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VOLUME 217 JULY 22, 1937 NUMBER 4

THE TREATMENT OF SEPTIC COMPOUND FRACTURES OF THE TIBIA WITH MAGGOTS

STEPHEN MADDOCK, M.D.,* AND DOROTHY JENSEN, A.B.†

BOSTON

DURING the past 7 years the writers have treated 44 cases of septic compound fracture of the tibia with maggots. Most of these were true compound fractures, but 10 cases were compounded by operation. A number of compound fractures of other bones have also been treated during this period, but since the results obtained with the tibia are neither our best nor our worst, and since in actual numbers the tibial fractures predominate, it seems worth while to dignify the series by a separate report.

All of the acute cases were previously operated upon by other surgeons and were referred specifically for maggots, either because the lesions failed to respond to the usual methods of treatment or because of interest in this form of therapy. Maggots were used during the period of most severe infection, and replaced by other measures as seemed to be indicated for the individual case.

In order to determine the end results, the patients have been seen at regular intervals after closure of the wound. Nearly all cases reported here have been examined clinically and by x-ray during the month of May, 1937. Sufficient data have been included to allow the reader to form his own conclusions concerning the method of treatment. No cases have been included in which treatment was begun after September, 1936.

Infected compound fractures of the tibia fall into several definite groups. For purposes of description the following classification will be used:

1. Acute sepsis.
   a. With avulsion of soft parts.
   b. Without avulsion.
   c. Following open operation.
2. Chronic sepsis.
3. Traumatic amputation.

The literature of maggot therapy has become so extensive since Baer's[1] original communication in 1929 that it is beyond the scope of this article to attempt a discussion of it. The reader is referred to the bibliography compiled by Robinson.[2]

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OPERATIVE TECHNIC

The surgical treatment of our cases varied with the individual surgeon. No attempt will be made to describe the technic used, since Hermann[3] will shortly publish in this *Journal* an analysis of methods at the Boston City Hospital. The description of operative procedure will be limited here to such features as directly concern maggots.

1a. Acute Sepsis with Avulsion. Badly avulsed wounds present the greatest problem because they can never be completely debrided, and there is always gross loss of soft parts in addition to bone injury. Since most of these wounds come from motorcar accidents they are often attended by shock, head injury or other complications which make immediate operative treatment dangerous if not impossible. Although none of the cases in this series were treated immediately, experience with acute compound fractures in other bones leads us to believe that maggots can be relied upon to remove devitalized tissue and foreign detritus from the wound more effectively and with less trauma than any method of irrigation or sharp dissection thus far discovered. The treatment can be started immediately upon the control of gross bleeding. No preliminary irrigation is necessary. As soon as the splints can be applied for immobilization, the larvae are placed in the wound and the area covered with gauze fluffs and cellucotton pads. This causes no more shock to the patient than the ordinary first-aid treatment, and the dressing need not be disturbed for 48 hours or longer. If the damage is severe enough to require amputation, the leg will be kept sufficiently clean to permit this operation at an optimum time without fear of a fulminating infection. The usual prophylactic doses of tetanus antitoxin and gas bacillus antiserum should always be given, and repeated several times if there is marked tissue necrosis.

1b. Acute Sepsis without Avulsion. Most of our cases of this type were originally treated by

debridement and primary suture of the wound. In many instances infection became apparent within a few days, but in some did not manifest itself until after the removal of internal fixation appliances. The early cases were treated by the removal of sutures, warm fomentations or irrigations with Dakin's solution. Maggot treatment was not started until it became apparent that the infection was not subsiding. In all cases maggots were implanted without additional operative procedure. The larvae were able to penetrate the wounds, and as they removed necrotic material, were able to gain ample access to the involved bone. Bands or plates were allowed to remain in position so long as they fulfilled their function. Occasionally counterincisions were necessary to secure adequate drainage.

1c. Acute Sepsis Following Open Operation. This condition is quite important because it constitutes one of the major disappointments of surgery, for the operator and patient alike. The treatment was essentially the same as for the preceding group. Stitches were removed and maggots implanted in the wounds. The bone grafts, bands or plates were not removed until they ceased to be useful.

2. Chronic Sepsis. The chronic lesions arising from septic compound fractures present a problem which is almost as difficult as that encountered in chronic hematogenous osteomyelitis. Neither the clinical picture nor the x-ray can be completely relied upon to differentiate normal and infected bone. When these cases present themselves for treatment it has become our custom to establish maggots in the sinuses or ulcerations for at least 3 to 4 weeks before operation. During this period a certain number of lesions will heal or progress far enough toward healing to demonstrate that there is no bone involvement. These cases are then prepared for skin grafts.

In the event of true bone involvement the maggots tend to demonstrate its location, and it is not unusual to find that this area does not correspond with the x-ray or clinical opinion. At times there is less but not infrequently more bone involved than was originally suspected. After the preliminary period of study a typical effacement operation is performed, all scar tissue and infected bone being removed. The wound is packed with vaseline gauze and a cast applied.

3. Traumatic Amputation. Generally no operation is required in this type of case. Maggots can be implanted at once as in cases with avulsion.

MAGGOT THERAPY

The technic of the culture of maggots has been described so frequently that it requires no repetition here. The methods published by Robinson[4] have been followed in all essentials, and are so simple that any laboratory can produce a constant supply of maggots with a few hours' work each day. The flies used were *Phormia regina* or *Lucilia sericata.*

In *acute cases with avulsion* the maggots are placed in the wound with sterile swabs without any preliminary measures, as indicated above. In *acute cases without avulsion* or in *postoperative infections* the wounds are irrigated with a 1:50 dilution[5] of tincture of iodine, U. S. P., in 0.9 per cent sodium chloride. This removes mechanically any pus, fibrin or detritus which has accumulated. The wound is then irrigated with a sterile suspension (about 0.25 per cent) of calcium carbonate,[6] which renders the invariably acid wound sufficiently alkaline to be attractive to the maggots, since they will not always survive in an acid medium.

In *chronic cases* this same procedure of irrigation is used before starting maggots. Where a preliminary operation has been performed a window is made in the cast and the packs removed on the tenth day.

Clinical Course. Enough maggots are implanted to cover comfortably the surface of the wound. After experimenting with various types of cages, it was found that the best results were obtained by packing the wounds lightly with gauze after inserting the maggots. The capillary attraction of the gauze ensures continuous drainage and avoids pooling of secretions or pus. The entire wound is then covered with fluffed gauze held in place with bandages. Cellucotton pads are finally placed over the dressing in order to absorb the excessive wound drainage.

In necrotic wounds, maggots will reach full growth in 2 or 3 days. Dressings are changed daily or every other day on all hospital cases, and a fresh supply of young larvae is added. The full-grown maggots crawl out of the wound to pupate and are caught in the gauze, making it easy to remove them with the dressing. Within 24 or 48 hours after establishing maggots the exudate from the wound should change from a thick acid pus to a thin alkaline serosanguineous secretion. This usually has a distinctive odor which is often slightly ammoniacal in character.

There are some cases in which it is very difficult to establish maggots because pus continues to exude from the wound for several weeks. These cases usually prove to have abscesses or joint involvement with inadequate drainage. By establishing proper drainage the maggots can usually be made to survive and before long the outpouring of pus will discontinue. At each dressing all sloughing tissues are removed that can be pulled

loose with forceps or wiped off with gauze. It is not advisable to do much cutting of the more resistant structures even though they seem necrotic, since bleeding is often produced and new channels are thus opened to infection. During the early period of treatment only completely loose sequestrums should be lifted out. Fragments of bone that are still attached to periosteum or muscle should be retained, and allowed to revascularize if possible.

In large wounds the maggots will quickly eat up the necrotic tissues in the center and congregate at the margins. It is important to keep the exposed bone, fascia or muscle from drying. This can be accomplished by covering these areas with glucose or urea crystals.[7, 8]

After a short time the denuded bone begins to show a pinkish blush. Within a few more days tiny islands of granulation tissue appear above the surface of the bone and gradually begin to coalesce. Granulations will also grow from the edges of the intact soft parts and advance slowly down the bare shaft. When this result can be obtained the prognosis is much more favorable. If a large area of tibia fails to put forth granulations, the outer layers of cortex are completely dead and more drastic measures are necessary. These should consist in drilling shallow holes or chipping with a chisel, and should be undertaken early in order to avoid massive sequestration or delay in healing. Occasionally one or more small islands of firmly attached bone will fail to granulate. These areas are usually insensitive and represent bits of eburnated or devitalized bone, which can be removed without anesthesia either with rongeurs or gouge. After their removal bleeding is stopped by pressure, and maggots can usually be continued at once or by the following day.

As soon as the entire surface responds with healthy granulations the wound should be prepared for skin grafts by warm soaks or Dakin's solution. If the marginal skin is allowed to grow over a large area it becomes tightly adherent to the bone, and consequently thin and nonresistant to abrasions. Skin grafts not only hasten healing but also obviate the dangers from the small traumas to which the shin is ordinarily subjected. At times the substitution of wet dressings results in a regression in the appearance of the granulations. The reinsertion of maggots will stimulate some of these wounds, but others never seem to become quite healthy enough to support a graft. In this event a search must be made for other underlying adverse factors in the absence of a definite bone lesion. These chronic obstinate lesions will be discussed in another communication.

Some 10 cases in the series were not seen while in the hospital but were given maggots after their discharge. It is possible to treat many of the more chronic wounds as ambulatory cases, changing the dressings three times each week. This situation is often very desirable, since it lessens the cost of hospitalization, greatly improves the morale of the patient and permits an early return to work.

RESULTS

The results of this study are summarized in Table 1, in which the 44 cases are arranged as in the classification given above, and numbered arbitrarily according to the length of time which elapsed between the fracture and the beginning of maggot treatment.

1a. Acute Sepsis with Avulsion. There are 9 cases in this group, of which 2 are healed, 2 died, 4 were amputated and 1 has been lost. The deaths were due to general septicemia which was present before beginning maggot treatment. Case 1 was streptococcal; Case 7 was staphylococcal in origin. Amputation was performed in 3 cases because the destruction of soft parts was so great that there was no possibility of restoring a useful leg. In the remaining instance the patient demanded amputation because of nonunion, although the leg showed a healed lesion at the time. Case 9 (recorded as lost) terminated maggot treatment with a nonunion of the tibia, due to the sequestration of 5 cm. of the whole circumference of the tibia with the loss of 17 cm. of the medial aspect. The remaining bone was apparently free from infection and covered over with granulations. The patient was readmitted and was being prepared for skin graft, but became psychotic and had to be sent to another institution.

The average time of treatment with maggots was 113 days. The average period of hospitalization during maggot treatment was 70 days. The average time from fracture to complete closure of the healed cases was 269 days.

1b. Acute Sepsis without Avulsion. There are 14 cases in this group, of which 13 are healed and 1 is still under treatment.

The patient under treatment (Case 22) had a severe infection following the insertion of a Lane plate. The major infection at the site of fracture has been healed for many months, but each screw-hole showed residual infection. A doughnut-shaped sequestrum has finally separated from each of them, and recent x-rays show no evidence of further bone involvement. There are still two superficial granulating wounds, which should heal shortly.

The average time of maggot treatment was 82 days. Five of the patients were not treated with maggots until after discharge. The average hospitalization of the other 9 cases while under maggot treatment was 60 days. There are no instances of nonunion or deformity. Ankylosis resulted in

Case 17 owing to compound dislocation of the ankle at the time of original injury. The average time from fracture to closure in the healed cases was 288 days.

The patient (Case 33) who came to amputation was a 16-year-old girl who had had a chronic bone infection following the curettage of a benign giant-cell tumor in 1929. The lesion finally underwent sarcomatous changes which were detected after numerous biopsies of the atypical granulation that filled the wound. Mid-thigh amputation was performed, and as yet no metastases have developed.

TABLE 1. *Septic Compound Fractures of the Tibia.*

Case No.	Age	Sex	Date of Fracture	Onset of Sepsis	Maggots Started	Maggots Stopped	Hospital Discharge	Result	
					Acute Sepsis with Avulsion				
1	22	M	1/12/35	1/12/35	1/15/35	1/21/35	1/22/35	Died	
2	21	F	12/ 6/34	12/ 6/34	12/14/34	2/ 6/35	6/ 5/35	Amputation	5/ 2/35
3	49	M	1/31/35	2/ 1/35	2/ 9/35	8/19/35	7/ 1/35	Healed	12/16/35
4	53	M	12/ 8/35	12/ 9/35	12/20/35	1/26/36	3/22/36	Amputation	1/26/36
5	42	M	3/ 1/35	3/ 3/35	3/19/35	1/ 2/36	9/18/35	Amputation	9/ 5/36
6	45	M	12/26/34	1/ 7/35	1/14/35	11/ 6/35	5/20/35	Healed	8/ 3/36
7	44	F	6/ 27/36	6/27/36	7/22/36	8/11/36	8/11/36	Died	
8	24	F	7/ 3/31	7/ 4/31	11/ 3/31	11/18/31	12/16/31	Amputation	11/22/31
9	40	M	11/22/34	12/ 3/34	3/19/35	6/10/35	5/21/35	Lost	
					Acute Sepsis without Avulsion				
10	46	M	1/28/36	2/10/36	2/17/36	4/17/36	3/20/36	Healed	3/ 1/37
11	20	M	3/13/35	7/25/35	8/ 9/35	9/15/35	9/25/35	Healed	10/ 7/35
12	62	M	4/24/33	4/29/33	5/29/33	7/28/33	9/ 1/33	Healed	11/21/33
13	36	M	4/ 1/33	4/17/33	5/ 8/33	7/ 1/33	7/ 1/33	Healed	4/24/34
14	35	M	6/13/35	6/30/35	9/23/35	12/23/35	7/ 9/35	Healed	10/ 3/36
15	60	M	3/19/35	4/ 8/35	4/29/35	6/26/35	5/18/35	Healed	9/ 4/35
16	50	M	12/14/32	3/ 1/33	3/14/33	4/21/33	4/25/33	Healed	11/23/33
17	52	F	11/ 7/35	11/ 8/35	2/22/36	3/ 9/36	1/27/36	Healed	12/16/36
18	52	M	4/25/35	5/ 2/35	8/14/35	9/ 3/35	6/ 4/35	Healed	6/ 1/36
19	12	M	9/16/35	9/20/35	1/22/36	2/24/36	3/ 6/36	Healed	4/14/36
20	36	M	3/ 4/35	3/20/35	7/23/35	10/16/35	6/28/35	Healed	11/22/35
21	58	M	12/21/30	5/ 1/31	5/15/31	9/ 1/31	9/ 1/31	Healed	10/ 2/31
22	45	M	7/17/35	7/25/35	1/ 6/36	5/18/36	6/12/36	Treatment	
23	20	M	3/ 8/36	3/13/36	11/11/36	11/27/36	3/25/36	Healed	12/ 9/36
					Acute Sepsis Following Open Operation				
24	12	M	12/ 1/35	12/ 5/35	1/15/36	2/12/36	4/ 7/36	Healed	10/ 7/36
25	69	M	1/27/36	3/ 6/36	3/14/36	6/10/36	4/11/36	Healed	1/ 6/37
26	12	M	10/ 8/36	10/26/36	12/23/36	1/18/37	11/ 7/36	Healed	2/ 1/37
27	54	M	2/ 1/36	5/14/36	5/26/36	5/29/36	5/15/36	Healed	8/17/36
28	58	M	9/19/31	11/ 5/31	1/28/32	4/22/32	6/18/32		
					1/10/33	3/ 1/33	5/23/33	Healed	7/ 6/33
29	16	M	3/18/35	4/26/35	8/26/35	10/20/35	5/30/35	Healed	8/17/36
30	52	M	9/ 6/34	3/28/35	4/26/35	6/14/35	9/26/35	Healed	1/29/36
31	29	M	4/15/31	9/ 2/31	1/ 2/32	6/ 9/32	1/15/32	Healed	11/16/32
32	56	M	12/10/31	11/10/32	11/26/32	12/23/32	12/20/32	Healed	4/22/33
33	16	F	7/17/29	10/12/29	3/ 7/34	2/ 8/35	7/12/34	Amputation	2/17/35
					Chronic Sepsis				
34	24	M	1/24/35	2/ 1/35	3/29/36	4/ 9/36	4/ 7/36	Healed	4/20/36
35	61	M	4/22/34	7/10/34	8/13/34	1/ 4/35	1/24/35	Treatment	
36	50	M	7/24/34	8/ 6/34	2/24/36	5/30/36	3/20/36	Treatment	
37	36	M	9/19/34	4/18/35	4/22/35	1/29/36	4/ 6/35	Healed	4/24/36
38	46	M	1/ 3/30	2/12/30	12/ 1/31	1/11/32	12/12/31	Healed	11/15/33
39	16	M	4/11/33	8/ 2/33	5/ 7/34	7/11/34	7/11/34	Healed	10/ 3/34
40	26	M	11/ 2/29	1/25/30	6/ 1/31	7/24/31	8/ 1/31	Healed	2/17/32
41	42	M	12/ 1/31	12/ 8/31	2/ 1/34	7/25/34	2/16/34	Healed	7/25/34
42	26	M	5/21/32	9/11/34	5/ 3/35	6/29/35	6/20/35	Healed	7/15/35
43	39	M	10/26/15	?	11/ 7/35	12/20/35	9/12/16	Treatment	
					Traumatic Amputation				
44	56	M	10/14/32	10/14/32	12/23/32	1/17/33	3/23/33	Healed Stump	

1c. Acute Sepsis Following Open Operation. There are 10 cases in this group, of which 9 are healed and 1 was amputated. There were 2 cases of nonunion.

Cases 32 and 30 developed infection following bone grafts for nonunion of simple fractures, and in both cases nonunion has resulted. The lesions have healed under

treatment, but the patients are waiting for another bone graft when danger of reinfection has been lessened by the lapse of time.

The average time of maggot treatment in the healed cases was 50 days. The average period of hospitalization during maggot treatment was 63 days. In 3 cases treatment was begun after discharge.

2. *Chronic Sepsis.* There are 10 cases in this group, of which 7 are healed and 3 are under treatment. The cases listed as under treatment may be considered briefly.

The first patient (Case 35) had a fracture of the left leg, and after leaving the hospital developed a right-sided hemiplegia associated with considerable dementia. The left leg still has two sinuses, which open up from time to time, but because of the inability of the patient to attend the clinic no consistent treatment of any sort can be carried out. He can be seen at his home occasionally, but the family refuses hospitalization. There is probably some small residual infection which could be cleared up in a short time with active treatment.

The second (Case 43) had an old compound fracture of the mid-shaft which has been draining since 1915. The patient was treated with maggots for 44 days in 1935 and then disappeared from the clinic. In answer to a letter he returned in 1937, but will not submit to either maggots or an operation. The leg shows two small areas of exposed necrotic bone. He is being treated by other methods.

The third (Case 36) had an extensive removal of bone for chronic sepsis. This has gradually filled in, and his physician reports that he expects healing within a few months.

There are no cases of nonunion or ankylosis. The average length of maggot treatment was 97 days and of hospitalization during treatment 47 days. Three patients were treated after discharge from the hospital.

3. *Traumatic Amputation.* The 1 case in this group had the lower half of the leg amputated in a train wreck. A severe mixed infection including gas bacillus developed, but the stump cleared up in 25 days and following reamputation has remained closed.

SKIN LESIONS

After the apparent healing of the bone it is not uncommon to have persistent areas of ulceration, varying in size from 1 to 5 cm. These generally present a flat, smooth, shiny granulating surface, free from pus or exudate. The usual wound stimulants fail to produce healthy granulations. These lesions have no connection with the bone clinically or by x-ray, and often occur at a distance from the actual fracture site. It is usually possible to heal these cases by ambulatory treatment, but bed rest greatly facilitates closure. Since these lesions cause no discomfort, the patient usually refuses to interrupt his work in order to attend to them. It has been customary to regard such cases as healed compound fractures, since there has never been any case which showed subsequent bone involvement, and since they all heal ultimately with persistent treatment.

Erysipeloid lesions of the leg and thigh with involvement of the lymph nodes in the groin are not uncommon during the course of the condition. These incidents incapacitate the patient for several days, and may be accompanied by chills and a temperature rise to 105°F. They never show serious manifestations and often seem to result in a hastening of closure.

Persistent eczema sometimes occurs after the healing of the wound. This dermatitis fails to respond to the usual washes and ointments, and it is only by experimentation with a number of remedial agents that cure is found.

CAUSES OF FRACTURE

The causes of fracture were: motorcars 23, falls 13, train wrecks 2, industrial accidents 2, open operations 3, explosion 1. The automobile in addition to being the most frequent traumatic agent also caused the most serious injuries, since 7 of the severe avulsions, the 2 deaths and 3 of the amputations fall into this group. Practically all of these patients were pedestrians who were either struck by bumpers or run over.

ECONOMIC STATUS

Before the injury the economic statuses of the 44 patients were: employed 29, school 9, on relief 6. During the course of treatment 21 returned to work, 6 returned to school, 2 died, 5 had leg amputations and 10 others are still not at work. These 10 patients are not working for the following reasons: nonunion 2, too old 2, cardiac disorder 1, able to work but too lazy 5. This indicates that a high percentage of rehabilitation is possible. Of 38 who were working or in school before injury, 32 (84 per cent) have returned or are able to return to their usual tasks.

RECURRENCES

In several of the cases superficial abscesses developed in the scar some months after healing was apparently complete. These were managed very conservatively and treated as purely soft-part infections. Several times maggots have been reinserted, but usually dry dressings have sufficed.

In one instance (Case 28) the patient left the hospital before closure occurred and was lost. He returned almost a year later with a large indolent granulating wound. Maggots were placed on this lesion, and as a result of their activities, several buried sequestra were found and removed. The wound healed after 6 months and has remained closed.

Another patient (Case 31) was kicked by a horse and sustained a transverse fracture of the mid-shaft on April 15, 1931. An open reduction and a Lane plate resulted in infection. He was treated with maggots from January 2,

1932, to June 9, 1932, and the wound healed completely on November 16, 1932. The patient was seen at intervals during the next 4 years. There was never any trouble with the leg. On April 16, 1937, he was struck by a heavy iron horse over the area which had previously been involved, and the tibia was denuded of periosteum for a space of 7 by 3 cm. Maggots were inserted, and the bone began to cover over with healthy granulation tissue within a few days. On May 18, 1937, a skin graft was performed, and the lesion closed on May 25. The patient was able to return to work on June 3, 48 days following the injury. No hospitalization was necessary.

Table 2, giving the average time consumed in the treatment of each group, presents a summary

TABLE 2. *Summary.*

Group Number	No. Cases	Healed	Under Treatment	Amputation	Died	Lost	Percentage Healed	Days: Fracture to Maggots	Days: Maggot Treatment	Days: End of Maggots to Closure	Days: Hospitalization During Maggots	Days: Total Time
1a	9	2		4	2	1*	25	44	113	112	70	269
1b	14	13	1*				100	99	82	107	60	288
1c	10	9		1*			100	140	50	224	63	414
2	10	7	3*				100	451	97	195	47	743
3	1	1					100	70	25	65	160	160
Total	44	32	4	5	2	1						

*Omitted in calculating average figures.

of Table 1. It will be noted that the period of treatment with maggots was relatively short, constituting only 10 to 12 per cent of the total period in the more chronic groups. A considerable period of time often elapsed between stopping maggots and the final closure of the wound. This is occasioned in part by our failure to skin graft all cases in the early years of this study, and in part by allowing the patients to become ambulatory before complete closure occurred. Actual healing of the bone occurred at the time of termination of maggot treatment in almost all cases.

DISCUSSION

The value of any therapy is determined by the quality of the end results and the time consumed in the treatment. The results in this series are open to several interpretations. If the 4 patients still under treatment and the 1 who was lost are excluded, the series consists of 39 cases, with 32, or 82 per cent, showing healed lesions. The writers, however, feel entitled to exclude some additional cases. Case 33 came to amputation because of malignancy, and Case 5 demanded amputation because of nonunion although the infection was healed. Cases 4 and 2 were recognized as hopeless and were only undertaken with the idea of improving the patient's general condition sufficiently to allow amputation to be performed. If it is justifiable to omit these 4 cases, the successful results are raised to 91 per cent.

Unfortunately there are no statistics available for comparison with regard to the time element. Authors who have written about infected compound fractures are very reticent concerning the actual time of recovery, and few have followed their patients for long periods after leaving the hospital. Table 2 shows that considerable time elapsed in many cases between the fracture and the beginning of treatment, but that in all groups the average time from the start of treatment to complete closure was about the same (6 to 8 months). One may infer from this that, if maggots are begun early, healing can be appreciably hastened.

The obvious disadvantages of maggots are expense, and discomfort to the patient. The expense of raising or buying maggots is not so great as it would seem if consideration is taken of the shortening of hospitalization, lessened nursing care and the elimination of chemicals and mechanical apparatus generally used. The actual time of maggot treatment in this series averaged only 84 days. Pain cannot always be eliminated, particularly in superficial wounds. A certain degree of pain seems to be psychic, since patients who are kept in ignorance of the nature of the treatment seldom complain. Children are always more amused than annoyed. By replacing large maggots with fresh cultures much of the pain can be avoided, since there is no discomfort for the first 24 or 48 hours. Nupercaine ointment (1 per cent) placed on any particularly sensitive granulations often eliminates discomfort.

Maggots seem to have several advantages over other methods of treatment of septic compound fractures. The most striking of these is the rapid dissolution of necrotic material and the disappearance of pus. During this period any attendant cellulitis becomes more localized, and temperature and pulse rate return to normal. The wounds respond quickly with fresh granulations, and the small islands of granulations which appear on bare surfaces of bone seem to survive better with maggots than with chemical applications. This is true of both acute and chronic wounds. In the latter, the stimulating effect of maggots on granulation tissue is particularly important because these wounds seem to lack the usual impetus to tissue growth, owing to frequent operations or prolonged sepsis. The continuous nature of maggot treatment is an important consideration. It is not dependent upon intrinsic factors such as the pH of the wound, or extrinsic variables such as nursing

care or pharmaceutical accuracy. The period of hospitalization and disability can be materially shortened as compared with irrigation methods. In situations where the general condition of the patient temporarily precludes inevitable amputation, general septicemia can be prevented by the early use of maggots.

Since most of the patients with septic compound fractures are adults, early rehabilitation is important both economically and psychically. In many instances in the group of cases presented here, healing time was sacrificed in order to allow the patient to return to work. This can be done easily with maggots since the treatment is not interfered with by many types of employment.

It is not the contention of this article that all compound fractures require maggots; fortunately the majority heal without incident. For the group of cases where sepsis is apparent and uncontrollable they seem to offer something that works where the commoner methods of treatment fail.

The word "healed" has been used in describing the present condition of the majority of these patients. This has been done advisedly because an adequately treated septic compound fracture once healed stays healed. Conversely, no draining compound fracture should ever become chronic. These patients can always be promised a cure if union occurs and if they are willing to submit to treatment. There is no reason to regard septic compound fractures with the pessimism that often greets chronic hematogenous osteomyelitis.

SUMMARY

A series of 44 cases of septic compound fractures and other infections of the tibia treated with maggots and followed up to the time of writing is presented. Thirty-two of these have healed lesions, 4 are under treatment, 1 was lost, 5 were amputated and 2 died. The deaths were due to general septicemia. The amputations were performed for the following reasons: gross loss of bone and soft parts 3, elective because of nonunion 1, and malignancy 1.

The management of wounds under maggot treatment is described. Maggots offer a good method for the treatment of these conditions. Their chief objections are expense and, in some cases, pain. Their advantages are rapid debridement of necrotic material, discovery of hidden sequestrums and pus pockets, stimulation of granulations, continuous treatment, shortening of hospitalization, and early rehabilitation. Chronic suppuration following infections of compound fractures, gunshot wounds or open operations should not occur. An adequately treated septic compound fracture of the tibia once healed stays healed.

It is a pleasure to thank Dr. Frederic J. Cotton, who originally suggested the use of maggots and was instrumental in obtaining technical assistance for producing them. Dr. Otto J. Hermann, the chief of the Orthopedic Service, has been especially co-operative. The writers are indebted to the following surgeons of the Boston City Hospital staff for referring cases: Drs. Binney, Walker, Kimpton, Cochrane, Fraser, Henderson, Shortell, Morrison, Burnett, Lucy, Peterson, Coonse, Bradford and Shannon.

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TUBERCULOSIS AT THE CROSSROADS

At the annual meeting of the National Tuberculosis Association, May 31, Dr. J. A. Myers was elected president and, in his analysis of the tuberculosis situation in this country as published in the July *Bulletin* of the association, the above caption is used to emphasize the fact that the decline in the incidence of tuberculosis seems to have been arrested.

Although the phenomenal accomplishments during the past thirty-five years in the reduced death rate stand as credits to the work of the association and the combined efforts of fifty-two state and large city associations and two thousand local societies, Dr. Myers warns all connected with this important phase of public health activity that "we must not be content that tuberculosis has been reduced so that its position as a cause of death may soon be compared with preventable diseases." He then claims that the agencies "are at hand for us to eradicate this disease from the list of human ills."

In order to re-establish the decline in the mortality rate of former years, it is clearly set forth by Dr. Myers that there is more need than ever to continue the work of the National Tuberculosis Association and that there must be a constant repetition of the facts concerning the disease and the elimination of obstructing factors such as carelessness, neglect and procrastination.

The article closes with the statement of Laennec which is applicable to all problems dealing with error and ignorance: "Do not fear to repeat what has already been said. Men need these things dinned into their ears many times and from all sides. The first rumor makes them prick up their ears, the second registers, and the third enters."

HYPOGLYCEMIA DUE TO INSULIN

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THE problem of "insulin reactions" is still an important one in the treatment of diabetes; the hope that they would practically disappear with protamine insulin has not been entirely realized. To be sure, considering the number of injections of insulin given daily throughout the world, the incidence of noteworthy reactions is actually very low. With protamine insulin, attacks are less frequent and come on more gradually, but they continue to be a possibility which worries the patient and his family and plagues the doctor. A brief review of the subject therefore seems timely and worth while.

CAUSES

The causes of hypoglycemia are well known: an overdose of insulin, too long an interval between insulin and food, too little or poor absorption of food or physical activity unusual for the individual. In this paper, conditions which are unrelated to diabetes but in which hypoglycemia may occur will not be discussed. These include prolonged muscular exercise, undernutrition and chronic wasting diseases, tumor of the islands of Langerhans, hyperinsulinism without tumor, hypopituitarism, hypothyroidism, Addison's disease, progressive muscular atrophy and extirpation of the liver (in animals) or extensive liver disease.

CORRELATION OF SYMPTOMS WITH LEVEL OF BLOOD SUGAR

Symptoms appear in the average diabetic patient receiving insulin when the blood sugar falls from a higher level to 0.07 per cent or below. Certain workers have described reactions with blood-sugar values well within normal range, but in only rare instances have we recognized an attack with a blood sugar higher than 0.08 per cent (Folin's methods of analysis have been used). For years in this clinic it has been an invariable rule in every reaction or supposed reaction to obtain blood for a sugar determination before carbohydrate is given. It is true that the rapidity with which the blood sugar falls has much to do with the level at which symptoms appear and the suddenness of their onset. This fact undoubtedly explains the lessened tendency for reactions with protamine insulin.

Maddock and Trimble[1] have shown that certain nondiabetic individuals may possess a definitely subnormal blood-sugar content—below 0.050 per cent and as low as 0.039 per cent—and yet be without symptoms. Similar findings have been reported by others.[2] It is an everyday experience that the degree of hypoglycemia necessary to produce symptoms varies from person to person, and in a given individual may even vary from one time to the next. The most striking case reported is that of Peters and Rabinowitch.[3] This was that of a man, aged 22 years, with diabetes of 4 years' duration. Random tests repeatedly showed him to have low blood-sugar values without symptoms. (It is true that during one attack of hypoglycemia he suffered a transient hemiplegia which persisted for 2 days.) Accordingly, to test this point, on a given day 10 units of unmodified insulin was administered and food was withheld. By 10:00 a. m. the true blood sugar had fallen to essentially zero and remained at this level until 4:00 p. m.! It is stated that no symptoms were present during this 6-hour period of aglycemia. Dr. Rabinowitch wrote to us on January 29, 1937, that "since our article in the *American Journal of the Medical Sciences,* we have had a number of patients who were practically aglycemic without symptoms."

At the Deaconess Hospital we have been interested lately in studying the true glucose content of the blood in some of the more severe reactions. It is well recognized that the values usually given for blood sugar represent not only the amount of glucose but in addition certain nonglucose reducing substances, chiefly glutathione and thioneine, in concentration of 15 to 30 mg. per cent. By determining the blood sugar before and after fermentation, this nonglucose fraction can be determined. Recently in 2 cases (Case 15295, male, aged 10.6 years and Case 9148, female, aged 14.6 years) with symptoms of severe hypoglycemia we have in this way found *true glucose values of zero* (actually 0.003 and 0.000 per cent, respectively). This might have been expected from the animal experiments of Dotti and Hrubetz,[4] who regularly found true blood-sugar values of zero in severe hypoglycemic reactions which were produced experimentally.

This brings up the question of the distribution of sugar between the red blood corpuscles and the blood plasma. In the past, some observers[5] attempted to explain the occurrence of supposed

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hypoglycemic symptoms in the presence of blood-sugar levels that were higher than normal by suggesting that whereas the sugar content of the whole blood was normal, the erythrocytes were impoverished ("cytoglycopenia"). The work of Olmsted[6] in the last 2 years has thrown discredit upon any such reasoning. He has shown conclusively that in vivo, even under normal circumstances, the red blood corpuscles contain no sugar whatsoever. After blood is shed, changes take place swiftly, and sugar passes quickly into the erythrocytes.

SENSITIVITY TO INSULIN

Individuals vary not only in the level of blood sugar at which they experience symptoms of hypoglycemia but also in their sensitiveness to insulin. A given dose of insulin may have very little effect on the blood sugar in one person and produce a marked fall in another. In general, patients with the severe juvenile type of diabetes are apt to be more sensitive to insulin than those patients in middle life with milder grades of the disease. Himsworth[7] has suggested a test for the differentiation of patients into these two types. His procedure is as follows. Control blood samples (capillary) are obtained after an overnight fast. Then measured amounts of insulin are injected intravenously and, immediately afterward, glucose is given orally in 250 cc. of water. The dosage used is 5 units of insulin and 30 gm. of glucose per square meter of body surface. Blood samples are taken at frequent intervals over a period of 90 minutes. The procedure may be further elaborated by taking samples of venous blood at intervals during the test, thereby permitting the determination of the capillary-venous difference. We have carried out a few such tests. The results obtained in two diabetic patients are contrasted in Figure 1.

It is obvious that Case 14375 is insensitive and Case 9769 is sensitive to insulin. In the first patient, the natural rise in blood sugar which follows the taking of glucose was affected little if any; in the second, not only was the blood-sugar rise minimal but it was followed by a definite depression of the curve.

It is important to call attention to the fact that cachectic patients, such as those suffering from advanced tuberculosis, cancer or other wasting diseases, may be extremely sensitive to insulin, and in these individuals hypoglycemia may follow relatively small doses of insulin. This presumably occurs because of the low glycogen reserves of such patients. In consequence the action of the insulin finds relatively little opposition provided by the hyperglycemia that results from glycogenolysis in the liver and muscles. Furthermore, the natural bodily defense against hypoglycemia, namely the secretion of adrenine, operates at a decided disadvantage because of the paucity of the substrate, glycogen. These facts point to the need for caution when using insulin in such patients.

SYMPTOMS AND SIGNS

We conceive of the symptoms of hypoglycemia as arising from the lack of sugar in the fluid bathing the fixed tissue cells of the body and most

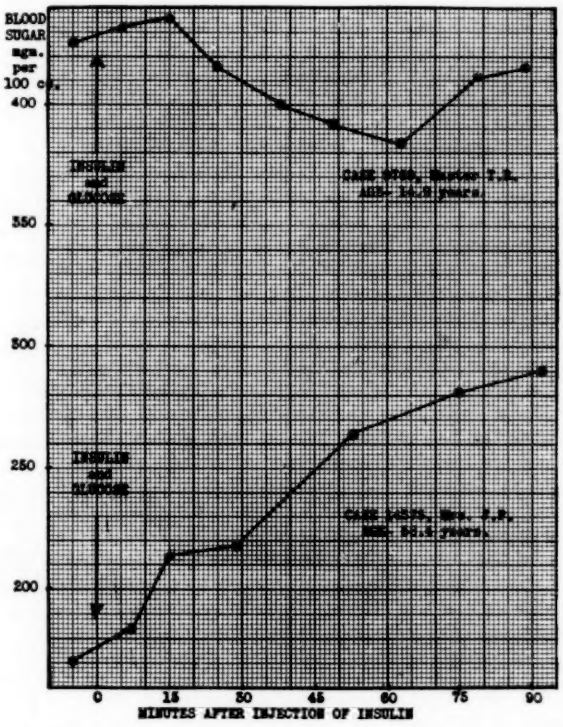

FIGURE 1. Curves illustrating differences in sensitiveness to insulin. Both patients received 5 units of insulin (intravenously) and 30 gm. of glucose (orally) per square meter of body surface. No food or insulin was given on the morning of the test.

Case 9769: Height, 55¾ in. (142 cm.); weight, 82 lb. (37.2 kg.); diet, C_{220} P_{105} F_{100}; insulin dosage, 92 units daily.

Case 14375: Height, 60 in. (152 cm.); weight, 155 lb. (70 kg.); diet, C_{140} P_{80} F_{75}; insulin dosage, none needed for control of diabetes.

particularly those of the nervous system. Ordinarily the sugar content of the intercellular fluid must be rather less than that of the blood, owing to the utilization of sugar in the tissues. Exactly why individuals may rarely have blood-sugar values of zero and still be asymptomatic is not clear unless one supposes, as does Rabinowitch,[8] that in such cases for some unexplained reason the tissue sugar is higher than the blood sugar.

Although reactions due to unmodified insulin commonly appear 3 or 4 hours after the insulin has been given, those produced by the slowly acting protamine-zinc insulin are most likely to occur within 12 to 24 hours after its administration. Patients receiving an overdose of protamine-zinc insulin usually have reactions during the night

or upon awakening in the morning. In our experience, however, the incidence of hypoglycemic attacks even during the night has been much less than under the former regimen.

Symptoms differ greatly from person to person and from reaction to reaction. Usually, however, a mild reaction is characterized by nervousness, trembling and sweating without apparent cause. Faintness, hunger, weakness, fatigue and pallor may be present. Occasionally paresthesias, affecting especially the mouth, lips or tongue, may be an early warning sign. Thus Case 3194 could invariably foretell a reaction by numbness and tingling of the lips. Definite signs of an outpouring of bodily adrenine in response to the low blood sugar is frequently evident from the rapid pulse rate. Coincident with the tachycardia there may be a rise in blood pressure, as has been demonstrated by Pijoan.[9] He gave 15 units of insulin intravenously to 25 fasting normal individuals and determined the blood sugar and blood pressure at frequent intervals thereafter. Usually within the first 40 minutes there was a drop in blood sugar to an average level of 0.03 per cent without noteworthy alterations in blood pressure. Then a sharp rise in blood pressure took place. This averaged 40 mm. of mercury, systolic, and 7 mm., diastolic, above the control readings. Even more striking changes were found in a similar study of 20 cases of essential hypertension with increases in systolic pressure averaging 70 mm. Incidentally, it is interesting to note that no blood-pressure changes were observed following the production of extreme hypoglycemia in 4 patients with Addison's disease.

Further evidence of the increased secretion of adrenine in response to hypoglycemia is furnished by our Case 3717. This patient, aged 29.1 years, with diabetes of 13.2 years' duration, notes amelioration of his severe bronchial asthma following a marked insulin reaction.

All of the signs and symptoms so far discussed may be attributed to stimulation of the autonomic nervous system. Less common symptoms which fall under this same classification are headache, nausea and vomiting. This triad has forced itself upon our attention only recently and since the introduction of protamine insulin. Presumably long-continued hypoglycemia is responsible. Even using unmodified insulin, we have at times seen marked occipital headache lasting for hours, as in Case 14483. This woman, aged 36.8 years, is a patient with insulin resistance who has taken from 300 to over 600 units of insulin daily for more than 1½ years. Occasionally children have exhibited nausea and vomiting with hypoglycemia that had been produced by protamine insulin. Such symptoms have led us to fear that at some time or other the differential diagnosis between diabetic coma and insulin shock may be confused. Gray and Burtness[10] found that in a group of 38 patients, 22 of whom suffered from true migraine, headache was present when the blood-sugar level was between 0.06 and 0.09 per cent. Frequent carbohydrate feedings afforded complete or partial relief of the headache.

Alterations as regards the circulatory system have already been mentioned. Other changes have also been described. These include extrasystoles, bradycardia rather than tachycardia, increase in circulatory rate and minute volume, and electrocardiographic changes characterized chiefly by a decrease in the height or an inversion of the T-wave. However, the last-named are, in otherwise normal individuals, slight, infrequent and inconstant, as has been shown by Dr. H. F. Root in this clinic. This agrees with the experience of de Châtel and Palisa.[11] They studied 19 schizophrenic patients without heart disease who were subjected to almost daily severe hypoglycemic attacks for months. Depression of the T-waves was the only abnormality noted, and this was by no means a constant finding. The electrocardiographic changes did not correspond to the severity of the insulin shock. One patient with a blood sugar of only 0.02 per cent (the true blood sugar was probably zero or nearly so) showed no alteration in the tracings.

In addition to the above, there are a group of symptoms and signs regarded by Wilder[12] and Falta[13] as due to influences upon the central nervous system. The development, through successive phases, of these features of profound insulin shock, such as those seen in schizophrenic patients with induced hypoglycemia, has been accurately studied and described by von Angyal.[14] Wilder divides the group into three parts depending upon the level of the brain stem and spinal cord involved: (1) bulbopontine; (2) corticospinal; and (3) striothalamic.

Chief among the bulbopontine signs are the slow reaction of the pupils to light and the disturbances of speech such as retardation and difficulty in formulating words. Thus Case 12069, an intelligent man of 51.2 years, twice recently was unable to carry on an intelligible conversation despite a great desire to impart some information. There was also an associated mental confusion, as is usually the case.

In the group of corticospinal symptoms are found some of the most distressing effects of a low blood sugar. They include incontinence of urine and feces as seen in our Case 14493, aged 37.2 years, whose blood sugar was 0.017 per cent at the time. In addition this patient had absent patellar reflexes and a bilaterally positive Babinski sign. This sign became normally negative within a few

minutes after relief of hypoglycemia. At least 5 of our patients (Cases 2856, 4697, 4115, 2052 and 3727), together with Case A. F. of Dr. F. G. Brigham, have had transient attacks of monoplegia or hemiplegia apparently brought on by hypoglycemia.[15] Muscular inco-ordination and an unsteady gait are occasionally seen. Tonic and clonic convulsions during severe reactions are not at all uncommon and if recurring in the same individual, may suggest the diagnosis of epilepsy. In a paper published in 1933 Jordan[16] discussed the differential diagnosis of epilepsy and hypoglycemic convulsions. This may at times present difficulties, and always calls for repeated determinations of the blood sugar at the exact time of the convulsive seizures. Double vision is frequently, and transient dimness of vision rarely, a symptom of hypoglycemia. Disturbances of taste and smell have been described.

The group of striothalamic symptoms include both those characterized by underactivity, as a staring gaze and inability to move muscles as desired, and by overactivity, as involuntary crying, smiling or laughing, grimacing, athetoid and choreiform movements and generalized muscular rigor. The inability to move muscles as desired was well illustrated in Case 7736, a young man of 24.2 years with diabetes of 8.3 years' duration, who at a cinema, sensing an impending reaction, thought about the two lumps of sugar which he had in his pocket, but was powerless to direct his hand to them. Somehow he found his way to the open air and walked a short distance, only to be picked up a few minutes later by policemen who took him to a hospital, where he was admitted as "an unknown white man with epilepsy." Later he had almost no recollection of the film shown at the cinema, and recalled only the feeling that he should reach for his sugar but could not.

There still remain those symptoms which reflect the effect upon the cerebral cortex. These are catatonia, delirium, irritability, perversity and tantrums in children, pugnaciousness, automatism, negativism, hallucinations, amnesia, psychoses of various types and partial or complete unconsciousness.

Unconsciousness of even a few hours' duration, if unaccompanied by convulsions, is without apparent damage provided the patient is kept warm. The chief danger lies in the possibility that the diagnosis of diabetic coma may be made and additional insulin given. This happened in our Case 12882, a young woman of 27 years, who, with very little warning, became unconscious within a few minutes after returning home from work in the late afternoon. She was thought to have diabetic coma and was given repeated doses of insulin, totaling 200 units, during the night. By morning, when the true diagnosis was suspected, the blood sugar was 0.028 per cent and the spinal fluid sugar was zero (the "true" blood sugar was probably zero or nearly so). Despite a constant infusion of glucose that raised her blood sugar to normal, she died without regaining consciousness. This case has been reported elsewhere by Root.[17] Aitken[18] finds that marked residual mental deterioration may occur in cases of hyperinsulinism despite total relief of the condition itself.

The psychoses which are sometimes seen may complete a picture which suggests alcoholic intoxication to the observer. It is too much to ask a policeman to suspect or recognize hypoglycemia when he sees an individual with staggering gait, double vision and mental confusion who speaks unintelligibly and resists measures intended to aid him. A patient in such a condition while driving an automobile is a menace to himself and to others upon the highway. Quite obviously it is hazardous for diabetics who are taking sizable doses of insulin to act as engineers, motormen, bus drivers, airplane pilots, switchmen in railway yards, crossing tenders, roofers, and so forth.[19, 20] Störring[21] states that among the last 1,200 diabetic patients treated with insulin in Umber's clinic in Berlin he observed 12 cases of hypoglycemia characterized by psychoses. He noted a tendency in any given patient for these psychoses to take the form to which the individual was hereditarily predisposed.

PATHOGENESIS

If, as stated above, the time of onset and the severity of symptoms of hypoglycemia cannot invariably be correlated with the level of blood sugar, what then are the other factors involved? Probably one is an inherent, constitutional difference between individuals, together with some degree of physical, nervous and mental fatigue at the moment. Another factor is the rapidity of fall of the blood sugar. With a slowly falling blood sugar more time is allowed for the response of adrenine. Coincident muscular activity plays a great part; if the subject keeps absolutely quiet the chances are less that symptoms will arise. A sudden stimulus, such as the noise from the clapping of hands, may precipitate a convulsion in a rabbit with a low blood sugar. When the midbrain is narcotized, however, rabbits tolerate hypoglycemia without convulsions. Mice will not convulse unless their body temperature is kept up to from 29 to 37°C.

In an attempt to elucidate the mechanism of the production of the neurologic symptoms in hypoglycemia, Dameshek and Myerson[22] produced insulin shock in patients with dementia praecox or dementia paralytica, and compared the sugar and oxygen contents of the blood in the vessels supplying the brain and an arm before and after the

giving of insulin. They concluded that during a severe hypoglycemic reaction the uptake of sugar by the brain is materially reduced, as is also the uptake of oxygen. They suggest that the neurologic symptoms of an insulin reaction may be due to the effects of a lack of oxygen on brain tissue. Anoxemia as a cause had been first suggested by Olmsted and Logan.[23] Dameshek and Myerson discuss the other theories which have been suggested to explain the mechanism of the neurologic symptoms. These include the adrenine theory[24, 25] and the theory of disturbed water balance.[26] It is most likely that an increased secretion of adrenine is responsible for certain of the symptoms of hypoglycemia, but it cannot be held responsible for the clinical picture seen in the advanced stages. Drabkin and Ravdin[26] suggested that insulin convulsions are related to an increased cerebrospinal fluid pressure resulting from anhydremia. Postmortem evidence from human cases lends some support to this view.

SEQUELAE AND FATAL CASES

What consequences may follow one or more attacks of hypoglycemia? Probably no mark is left by mild attacks, although we believe that no patient should be allowed to have even these frequently. Unconsciousness not attended by convulsions is not in itself of serious significance. Attacks with convulsions, particularly if recurrent, should certainly be prevented. We have followed with interest the reports of others regarding the recently introduced treatment of schizophrenia with repeated, severe hypoglycemic attacks brought about by large doses of insulin.[27] Time will decide whether such therapy is of real value. It may be that its sponsors are correct in believing that it is better to subject an individual to marked hypoglycemic crises with some hope of improvement than to allow a hopeless condition to run its course. However, experience with diabetic patients has shown how distressing such reactions may be to the patient, and one is loath to produce them deliberately unless the indication is unequivocally clear. Those using this form of treatment should report all deaths. It seems fair to suggest that three criteria must be satisfied: (1) that the diagnosis of schizophrenia can be made with sufficient accuracy to prevent the unwarranted treatment of patients with mental disease of a less serious prognosis; (2) that the mortality from repeated, severe hypoglycemic attacks is negligible; and (3) that, judged from the vantage point of months or years later, improvement of a definite and lasting nature can be achieved.

It is true that only rarely has insulin hypoglycemia resulted fatally. If one combines the two series of fatal cases which Bowen and Beck[28] and Sigwald[29] collected from the literature in 1932, one finds a total of only 32. Furthermore, if one studies the case reports one is forced to conclude that some patients of this small group died not from hypoglycemia but from a complicating condition. Since 1932 a few fatal cases have been reported, but it is fair to state that it requires unusual conditions or poor treatment, or both, to cause death in association with insulin hypoglycemia.

Postmortem findings, particularly in experimental animals, include hyperemia, edema and hemorrhages of the brain. This suggests that hypoglycemia may be accompanied by a disturbance of the water or electrolyte balance. In the fatal case reported by Bowen and Beck[28] there was extreme edema of the brain and spinal cord.

Although it is undoubtedly possible to precipitate attacks of angina pectoris or even of coronary thrombosis by the production of hypoglycemia in an individual with coronary disease, this should not discourage the careful use of insulin in such diabetics. If treatment is carefully planned, glycosuria can be abolished and the blood sugar kept at a satisfactory level without danger. We were recently much relieved to find that Case 1500, in which death was said to be due to a hypoglycemic attack, had at postmortem examination a typical coronary occlusion in which insulin certainly played no part.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of hypoglycemia and diabetic coma in the unconscious patient may at times present difficulties. We have seen mistakes in diagnosis each way: in one striking instance (Case 12882), already referred to, insulin shock was incorrectly diagnosed as diabetic coma, repeated doses of insulin were given, and death occurred. In another (Case 2967), profound diabetic coma was mistaken for insulin shock, glucose but no insulin was given, and the patient died within 2 hours of his admission to the hospital. In the accompanying table are summarized points helpful in the differential diagnosis.

We consider that laboratory confirmation of the diagnosis is absolutely essential. However, in the event that the unconscious patient is encountered in the home and it is extremely difficult to obtain laboratory aid quickly, it is justifiable to inject 20 cc. of a 50 per cent sterile, buffered solution of glucose intravenously. If the patient is suffering from insulin shock, the chances are great that this procedure will cause prompt and definite relief of unconsciousness. It is imperative to insist that recovery must be prompt and unmistakable, because patients with diabetic coma may often seem to

improve slightly with the giving of glucose intravenously.

TREATMENT

Prophylactic. It is important to realize that in anticipating a reaction it is preferable to give food that requires digestion. Whereas in the treatment of a reaction already present one wishes the prompt effect which sugar, orange juice, and so forth produce, in prophylaxis one desires a slow absorption of sugar from the digestive tract into the blood stream over a period of hours so that a prolonged effect and hence protection may be secured. For this purpose bread, crackers, meat or nuts are preferable.

TABLE I. *Diabetic Coma vs. Hypoglycemic Coma. Differential Diagnosis in the Unconscious Patient.*

Diabetic Coma	Insulin Shock
History	
Slow onset over a period of hours or days. Brought on by dietary indiscretions, inadequate insulin dosage, infections, thyrotoxicosis, or may appear as the first sign of a hitherto unrecognized diabetes. Onset often with marked thirst, nausea, vomiting, abdominal pain. Then follow rapid, deep breathing and drowsiness, leading to unconsciousness.	Rapid onset over a period of minutes (although with protamine-zinc insulin may come on more slowly). Brought on by too much insulin, too little or poorly absorbed food, or physical exercise unusual for the patient. Nausea and vomiting are uncommon.
Physical Findings	
Body temperature is subnormal unless infection is present. Skin is dry; mucous membranes and tissues show signs of dehydration; eyeballs are soft. Patient appears extremely ill; may be restless and moaning, as with pain. Respiration deep and labored (Kussmaul) except in preterminal stages. Pulse weak and rapid; blood pressure tends to be low.	Body temperature is usually normal. Skin moist; clothing often soaked with perspiration. Normal hydration of tissues; tension of eyeballs normal. Convulsions may be present. Respiration normal. Blood pressure tends to rise in certain stages.
Laboratory Findings	
Much sugar, acetone and acetoacetic acid in blood and urine. Plasma CO_2 low.	No sugar in urine (second specimen), low blood sugar, normal plasma CO_2.
Treatment	
Insulin, fluid, salt, glucose and supportive measures produce gradual improvement.	Glucose parenterally brings about prompt recovery.

Remedial. Treatment in an existing reaction consists in supplying carbohydrate in an easily available form, such as sugar, orange juice, ginger ale, candy or syrup. Usually this can be given orally with prompt relief. If the patient cannot co-operate, then 20 cc. of a sterile, buffered 50 per cent solution of glucose may be given intravenously. Often the patient regains consciousness before all of the solution has been injected. If this is not available, a sterile 5 per cent solution of glucose may be given subcutaneously. Sugar-containing fluid may be given by stomach tube provided care is taken in passing the tube; often, however, in patients in insulin shock gastric tone and motility may be such that little or no absorption takes place. Adrenalin or pituitrin in a dosage of 0.5 cc. given subcutaneously may often arouse an unconscious patient enough so that food may then be taken by mouth. In the reactions due to protamine-zinc insulin, reasonably enough, the patient may at times suffer a relapse of symptoms and repetition of medication may be required.

SUMMARY

1. Hypoglycemic reactions present an important problem in the treatment of diabetes with insulin. In a brief review of the subject the signs and symptoms, pathogenesis, differential diagnosis in the unconscious patient and treatment are discussed.

2. There is considerable individual variation in sensitivity to insulin and in the level of blood sugar at which symptoms of a reaction occur.

3. Two cases of marked hypoglycemia with true blood-glucose values of zero are reported.

4. To establish the cause of unconsciousness in a diabetic patient, full use of all available laboratory aid should be made promptly.

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CHICKENPOX ENCEPHALITIS

Report of a Case

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ALTHOUGH encephalitis is well recognized as a complication of vaccinia, measles and smallpox, its occurrence in chickenpox has only recently been brought to the fore. A suggestion as to the frequency of this complication is found in Bullowa and Wishik's[1] recent paper, in which they state that there were 5 cases of encephalitis out of 2,534 cases of chickenpox at the Willard Parker Hospital in New York City in the period between January 1, 1929, and December 31, 1933.

An article by Underwood[2] has appeared during the past year in which the author reports a case of his own and discusses at length 119 others compiled from the literature. Mainly on the basis of the predominant symptomatology in each case, he classifies the neurologic manifestations as prodromal features, meningoencephalitis, encephalitis, myelitis, neuritis, ocular manifestations and other conditions. The encephalitic group is subdivided into cerebral, acute cerebral tremor, cerebellar, choreoathetotic and noncharacteristic forms. The myelitis group may be typical (ascending or transverse), anterior poliomyelitic or multiple sclerotic.

The spinal fluid was clear in the 58 cases where it was recorded, but in 2 cases there was xanthochromia. The pressure was normal in 20 cases, slightly increased in 10 and markedly so in 12. The cells were normal in number or only slightly increased in 31 cases and markedly increased in only 4. Of the 109 patients where the outcome was recorded, 12 died and 15 had sequelae.

The severity of the chickenpox eruption appears to bear no relation to the occurrence of nervous complications.

CASE REPORT

A 3-year-old boy was referred to the Haynes Memorial by his family physician, Dr. Robert J. Donovan, on March 12, 1935, with a diagnosis of chickenpox and encephalitis. There was no history of any previous disease. A week before entry to the hospital, the patient and his three brothers developed chickenpox. In all four children the illness was mild in type, with a slight febrile reaction and a few typical lesions. The course of the disease was uneventful in all four until the afternoon of the day of admission, when the patient under consideration developed twitching of the extremities and became "wobbly" on his legs and subsequently unable to stand.

The physical examination on admission revealed a well-developed child lying quietly in bed. The pupils were equal, regular and reacted to light. There was no nystagmus. The eardrums were normal. There was no stiffness of the neck or back. The abdominal and cremasteric reflexes were equal and active. The ankle, biceps and triceps jerks were not obtained. The right knee jerk was slightly more active than the left. Kernig's sign and ankle clonus were absent. There were late, crusted lesions of chickenpox scattered sparsely over the body. On standing, the patient wavered and wobbled about, but no definite muscular weakness was made out.

The temperature was normal. Examination of the blood revealed a hemoglobin of 80 per cent (Tallqvist). The red blood-cell count was 4,850,000 and the white blood-cell count 12,600, with 51 per cent polymorphonuclears, 44 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophils.

On the second day the patient showed coarse, wagging movements of the head on sitting up, apparent ataxia on standing and a coarse intention tremor of the left arm. He was lethargic, with a stolid facial expression. The neck was very stiff; Kernig's sign was negative. The knee jerks were equal and diminished. The grip was good with both hands, and no definite muscle weakness could be determined. The eyes were normal. The cerebrospinal fluid obtained by lumbar puncture showed an initial pressure of 10 mm. of mercury (136 mm. of water). The fluid was clear and colorless. No cells were found on microscopic examination. The globulin was normal. The colloidal gold and the Wassermann tests were negative.

On the third day, the patient's facial expression seemed brighter, the neck was not rigid and Kernig's sign was not present, but he articulated poorly and was unable to stand.

On the fifth day the temperature, which had been elevated following admission, reached its highest point (100° F.), and the heart rate was 125 per minute. He responded slowly when spoken to. There was ataxia on standing, and he exhibited an intention tremor of the

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left arm. No weakness of the muscles could be determined.

On the seventh day, although still inactive and somewhat lethargic, he was able to stand, when supported, without wobbling. On the eleventh day, the neurologic manifestations had practically disappeared. He was discharged on the following day. Subsequently, when seen by his family doctor, he appeared normal, and no residual neurologic signs were detected.

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PROGRESS IN PEDIATRICS

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ONLY five subjects have been selected in this summary of the advances in pediatrics for 1936, and of these, three pertain to general medicine rather than primarily to pediatrics. Each of these subjects,—para-aminobenzenesulfonamide, mandelic acid, and the Davies-Hinton test for syphilis,—however, is so important to the practice of pediatrics that comment seems called for.

PARA-AMINOBENZENESULFONAMIDE

Although Heidelberger and Jacobs[1] described the bactericidal effect of para-sulfonamide benzeneazo compounds in 1919, it was not until 16 years later that these studies were applied to animal experimentation by Domagk.[2] This investigator injected hemolytic streptococci of human origin intraperitoneally into 26 mice. One and one-half hours later 12 of the 26 received one dose of prontosil by stomach tube; these 12 survived, whereas 13 of the 14 untreated mice died of streptococcal infection within 4 days. Further evidence to support these observations was soon offered.[3, 4, 5, 6]

As one might expect, there soon appeared numerous articles referring to the successful application of this dye to human beings suffering from streptococcal infections such as puerperal sepsis, erysipelas, streptococcal pneumonia, arthritis and so forth.[7–14] However, as has been pointed out,[15] these various authors failed to consider that spontaneous recovery from such infections is not unknown, and that the spectacular results could not in every instance be ascribed to the effect of the substance administered. More careful laboratory studies and clinical observations[15, 16, 17, 18, 19] have, however, demonstrated the value of para-aminobenzenesulfonamide and its derivatives in the treatment of individuals suffering from infections with beta-hemolytic streptococci. Animal experimentation has also indicated that it may be of value in the treatment of meningococcal infections,[20] but there is no evidence to indicate its value in infections due to the pneumococcus or staphylococcus. The mode of action of the drug has not been definitely established, although the consensus appears to favor a bactericidal effect.[18, 21, 22, 23, 24]

At the present time, the dye may be obtained commercially in the following forms: prontosil solution, which is a 2.5 per cent aqueous solution of a complex diazo dye from which sulfanilamide is liberated following its injection; prontylin, which is a tablet containing 0.3 gm. (5 gr.) of the active principle, sulfanilamide; and the basic salt, para-aminobenzenesulfonamide, which is a white crystalline substance having a solubility of about 0.8 per cent.

When prontosil solution is employed, the dosage for the first day should be 1 cc. per pound of body weight, administered subcutaneously or intramuscularly in 4 to 6 doses. Prontylin tablets, containing the active principle, sulfanilamide, are intended for oral administration, the initial dose of the preparation, based on body weight, being approximately as follows:

Pounds	Dose
Under 20	0.6 gm. (10 gr.)
20-40	0.9 " (15 ")
40-60	1.2 " (20 ")
60-80	1.5 " (25 ")
80-100	1.8 " (30 ")
100-120	2.1 " (35 ")
Over 120	2.4 " (40 ")

The *maintenance dose* should be calculated on the basis of 0.05 gm. (¾ gr.) per pound of body weight per 24 hours and should be divided into 4 or 6 doses.

The basic salt, which is always given by hypodermoclysis, should be freshly prepared with normal salt solution for each administration, as the sulfonamide tends to precipitate in a crystalline form when the solution is allowed to stand at room temperature. Such solutions are rarely used outside the hospital. The dosage of this preparation according to body weight is as follows:

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Pounds	Dose
Up to 40	0.8 gm.
40-80	1.6 "
80-120	2.4 "
Over 120	3.2 "

The method of treatment as well as the preparation employed varies according to the severity of the infection. In *severe infections* it has been found advisable to give the estimated dose immediately by hypodermoclysis, or if there is no gastric disturbance and the patient can swallow, to give the initial dose of prontylin tablets as previously described. If the condition of the patient is such that the tablets cannot be administered, the full dosage of prontosil solution should be given 4 hours after the hypodermoclysis. After the first 24 hours the administration of either the tablets or the prontosil solution should be continued until there is definite clinical improvement. The dosage of the tablets may then be decreased by one half or one third the original dose and continued for a period of from 1 to 3 weeks. If both prontosil and prontylin are being used, the dose of the former should be reduced by 50 per cent after the first 24 hours.

In *moderate* infections, one should employ the initial dose of prontosil solution or prontylin tablets. During the first 24 hours, the estimated dose or from one half to three fourths this dose should be given, the dosage being decreased as clinical improvement is shown.

Toxic manifestations, such as acidosis, tinnitus aurium, general malaise and methemoglobinemia,[25] may occur during the administration of the dye, and if such signs appear, the dosage should be reduced. It is advisable to discontinue the drug in the presence of agranulocytosis, jaundice or renal impairment or irritation.

Although the administration of para-aminobenzenesulfonamide appears to be of value in certain conditions, no procedure or form of therapy that appears to be effective in many different disturbances can be hastily accepted without the possibility of subsequent regrets. Both the experimental and the clinical data reported, however, suggest that the therapeutic results of the administration of this dye may eventually prove more effective than the dyes employed in the past but now discarded. This drug should certainly be introduced in the treatment of only those infections for which there is reasonable evidence of its value. Its indiscriminate use in all forms of infection may lead to its early and unwarranted discrediting.

BASAL METABOLISM

The proper interpretation of the basal metabolism studies of infants and children has been more confusing to the average pediatrician than one cares to admit. This is probably due to the fact that the standards established by various observers have offered too many different modes of evaluation. As a further source of confusion, the results of the best standards have not always been consistent with clinical experience, and this has done much to arouse doubt as to the real value of the procedure. Failure to comprehend fully the metabolism reports is, no doubt, largely due to our inability to understand the various factors that may and do influence the determinations. As Talbot[26] points out, the discrepancies may be due to faulty technic, failure to obtain a *true basal* rate or failure to take into consideration the various physiologic reactions for different ages and groups. No doubt it is this situation that led him to state: "I have attempted to approach the problem anew in order to weigh and compare the evidence, . . . to find where errors can occur and to co-ordinate the findings and select a standard that will be consistent with clinical experience."

Although many theories of the physiologic basis of heat production have been suggested, few of them have proved capable of practical application to infants and children. Since it is generally believed that the production of heat and energy is primarily dependent on active protoplasmic mass, the interpretation of metabolism studies in conjunction with creatinine excretion has been suggested[27, 28] as a more accurate method than those usually employed. When one considers that creatinine excretion is a reliable index of protoplasmic mass, and that its elimination is quite uniform from day to day, the possibility of employing it as a method of determining heat production appears promising. With these views as a basis for his study, Talbot[26] states: "In the choice of standards for children, there is much to be said for the simplicity of the weight standard which can be used for infants, children and adults. It has the added advantage of giving results which are consistent with clinical experience."

As previously mentioned, Palmer, Means and Gamble[28] obtained data on the creatinine excretion of adults as regards muscular activity. Recently, N. B. Talbot[29] has carefully investigated this aspect of metabolism in a group of children, and has shown that the evaluation of basal energy on the basis of the excretion of creatinine for a 24-hour period may yield more accurate information than the standards commonly employed. The fact that these studies were made during a period of active growth adds further significance to the results. Their continuation should throw light on the practical application of basal metabolic determinations in infants and children.

MANDELIC ACID

In 1931, Helmholz[30] noted that specimens of urine obtained from patients who were receiving

an effective ketogenic diet did not exhibit the same tendency for bacterial growth as did specimens received from individuals allowed an unrestricted diet. Subsequent studies revealed that urine from the former patients not only inhibited bacterial growth but in many instances were bactericidal; this action was more effective against the organisms of the typhoid-dysentery group than against other bacteria. Fuller[36] demonstrated that such action was directly proportional to the amount of beta-hydroxybutyric acid present in the specimen, and that this acid was effective only at a pH of 5.5 or less. The possibility that the ketogenic diet might be of value in the treatment of pyuria soon presented itself, and its clinical application quickly established its effectiveness in the treatment of certain urinary infections.[31, 32, 33, 34, 35]

As a result of the study of various organic acids with a structural formula somewhat similar to this acid, Rosenheim[37] found that mandelic acid was not only as effective a bactericidal agent as beta-hydroxybutyric acid, but that when given by mouth it was excreted unchanged in the urine. These observations were supported by Helmholz and Osterberg,[38] who demonstrated that concentrations of mandelic acid varying from 0.25 to 1 per cent could be readily established in the urine, and that within this range the acid would have a bactericidal effect on most organisms, provided the pH of the urine was properly adjusted.

The clinical application of mandelic acid was soon attempted by Lyon and Dunlop[39] on 16 patients with severe intractable urinary infections; 12 of these patients were "cured" within 5 to 12 days, and 2 of the remaining patients, who were tuberculous, became free of their secondary infections. The importance of continuing the treatment for several days after the urine has become sterile was stressed by these observers, for if therapy is withdrawn too early, recurrences may develop. Since these findings were published, numerous reports[40, 41, 42, 43, 44, 45] confirming the therapeutic value of this form of treatment have appeared.

Although the oral administration of mandelic acid greatly simplifies the treatment of pyuria due to colon bacillus infection and obviates the necessity of giving the patient an unpleasant diet, it does not preclude the importance of carefully studying the individual before such therapy is instituted. Catheterized specimens of urine should be obtained and bacteriologic examinations of these specimens made in order to determine the nature[46] of the infection. Pyelograms should be made, when indicated, to exclude the presence of calculi, tuberculosis, pyonephrosis, congenital anomalies, and so forth. The acid should not be employed until the underlying cause of the infection has been ascertained, as excessive therapy may destroy renal function and even cause death.[47] Care should be exercised in administering the acid to patients who already have a lowered kidney function, a condition which can be determined only by a careful examination prior to treatment.

The dosage of mandelic acid employed in the treatment of infections of the urinary tract varies according to the age and weight of the patient and according to the urinary output when the individual is given a restricted amount of fluid. The dosage, as suggested by Newns and Wilson,[42] has not always been found adequate, and the following dosage and fluid restrictions have been suggested:

Age	Total Fluid Intake (maximum)	Ammonium Mandelate (daily dosage)
Infancy	350 cc.	3 gm.
2-5 yr.	500 "	5 "
6-8 yr.	600 "	6 "
9-12 yr.	800 "	8-10 "

Because it was necessary to give ammonium chloride in conjunction with mandelic acid in order to obtain the proper pH in the urine, many patients suffered from nausea and vomiting. While this may not be an important factor in the treatment of adults, it not infrequently interferes with the administration of a drug to young infants and children. In order to avoid this unpleasant feature, the acid has been made available in the form of the ammonium salt, thereby making it unnecessary to administer ammonium chloride to acidify the urine. Although ammonium mandelate may be weaker than mandelic acid, the necessity of administering two unpleasant substances can be avoided. However, there have been instances in which it was difficult to maintain the proper pH in the urine throughout the entire day when the ammonium salt was given, and in such cases it may be necessary to employ ammonium chloride and mandelic acid in order to obtain the full therapeutic effect.

ASCORBIC ACID

Progress in a given subject is not necessarily scientific, for the milestones of advance should lead to but one ultimate goal, namely, its practical application to the patient. The observations of Szent-Györgyi,[48] King and Waugh[49, 50, 51] and Wolbach and his associates[52, 53] established the clinical nature and physiologic importance of vitamin C in the diet of the normal individual. As a result of this basic knowledge, various practical aspects have been determined, such as the effect of drying,[54] freezing,[55] storage,[56] canning[57] and cooking[58] on the vitamin C content of foods, with the result that foodstuffs so prepared may now be consumed with-

out fear of their vitamin content having been destroyed.

The next practical step lay in the preparation of this vitamin in a concentrated form. This was soon accomplished, and it can now be obtained from pharmaceutical houses for either oral or intravenous administration for those unable to receive a diet containing an adequate amount of vitamin C, or for those who have developed the clinical manifestations of its deficiency. The application of this practical measure is more important than is indicated by a casual glance.

First, there is the economic aspect. Infants suffering from scurvy are encountered in clinics more frequently than those suffering from rickets. The exact requirements of vitamin C have not been definitely established, although it is commonly considered that 25 mg. for infants and children and 40 mg. for adults is an adequate daily amount for prophylactic measures. These amounts should probably be doubled during the presence of acute or chronic infections.[59] Since 1 oz. of orange juice contains approximately 15 mg. of ascorbic acid, an infant must ingest and retain the juice of one large or two small oranges each day if scurvy is to be prevented. With the cost of good oranges varying from 29 to 65 cents per dozen, this soon becomes an expensive item to a family of limited means. Ascorbic acid can be obtained in tablets (25 mg. or more per tablet) for less than 2 cents each, and it is reported that this price will soon be markedly reduced. The practical application of this inexpensive source of vitamin C applies not only to families but also to institutions whose budgets for food are limited. It is true that there are less expensive fruit juices containing this vitamin, but none of them have it in the proportion found in naturally ripened oranges.

The infant who refuses orange juice or who vomits it whenever given must also be considered. In such a feeding problem, the tablets prove effective as an antiscorbutic substance. The same is true of infants unable to ingest orange or tomato juice on account of allergic manifestations. As a result of modern refrigeration, fresh fruit can usually be obtained in most localities; however, there are occasions when the opportunity to obtain large amounts of vitamin C in a concentrated form, uninfluenced by weather or time, proves of inestimable value.

DAVIES-HINTON TEST FOR SYPHILIS

During the past 2 years the diagnosis and treatment of syphilis have received nation-wide attention and efforts have been made to select a serodiagnostic procedure that would not only possess a high degree of specificity and sensitivity but would at the same time be practical. The recent evaluation of serodiagnostic tests for syphilis conducted under the auspices of the United States Public Health Service[60] has demonstrated what appears to be an outstanding sensitivity (91.9 per cent) and specificity (100 per cent) of the micro-Hinton test as developed by Davies.*[61] A recent editorial in the *Journal of the American Medical Association*[62] concerning the efficacy of these tests states: "Special note should be made of the apparent efficiency of a micromodification of the Hinton test." This micro method has been devised and controlled over a period of 2 years, and at the present time it seems ready for practical use.

The usual Hinton test, which requires 0.6 cc. of human serum, has been so modified that 0.05 cc. is sufficient for an accurate examination. Another practical feature of this test is the ease and simplicity with which the blood may be obtained. With a sharp V-shaped blade (Bard-Parker No. 11) the finger of an infant, child or adult is pricked fairly deeply and hung in a dependent position. With blood expressed from this skin puncture, 2 capillary tubes measuring 1.25 to 1.5 mm. in inside diameter are filled and then sealed with a flame or with sealing wax. The tubes are of such a length that they may be transported to the laboratory in a regular Wassermann tube. As may be seen, this manner of obtaining the specimen makes it no longer necessary to resort to venipuncture, a procedure which is not without its difficulties when one is dealing with infants or with obese individuals. Furthermore, the short period of time required to collect the sample renders the measure applicable to all patients seen in a busy outpatient department, thereby increasing the opportunity of detecting previously unsuspected cases of syphilis.

The Davies-Hinton test shares in general the advantages of flocculation tests over complement fixation tests: it is unnecessary to maintain laboratory animals, and there are fewer variable factors. The micro test employs the same indicator (glycerinated beef-heart extract) as the usual Hinton test. Unlike the material used for most flocculation tests, such as the Kahn and the Kline, this indicator, once prepared, may be kept for at least a month in the refrigerator without demonstrable deterioration.

The sensitivity of the test in capillary tubes may be due in part to its being carried out in sealed tubes, thus minimizing evaporation. This feature enables one to make the final readings after an incubation period of from ½ hour to 16 hours, depending on the clinical urgency or the convenience of the laboratory. Since the "positive" floccules rise to the top of the fluid column in the narrow tube, they are concentrated in a small

*"Sensitivity" refers to the ability of a test to detect cases of syphilis in its various stages; "specificity" refers to absence of false-positive reactions.

space, and minimal reactions are the more readily observed.

The results of the evaluation series mentioned above were based on a procedure involving an incubation period of 16 hours. Further studies have shown that entirely comparable results can be obtained after an incubation period of only 30 minutes. This "rapid" method lends itself to situations where a report is desired within a short period of time, such as before emergency transfusions, and should extend the usefulness of the test.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 23291

PRESENTATION OF CASE

A 5-year-old boy was admitted complaining of generalized edema.

The child's past history was noncontributory. He had had whooping cough at the age of 2 years and measles at the age of 3. Neither was accompanied by complications. There were infrequent head colds occurring about once a year.

About a month before entry the patient's parents noticed that he appeared to be "swollen" when he arose in the morning, although he had been normal the night before. The swelling was generalized but was most marked in the hands and feet. He was not kept in bed but was allowed to play in the yard. No urinary abnormalities were noted at this time. The edema disappeared in about 2 days, and the patient felt well during the succeeding week. At the end of this time, he again developed generalized swelling, most marked in his face and legs. He did not appear to be sick and again was allowed to play as usual. The edema persisted with variation in intensity until 2 days before entry. At this time it became more severe, and he was taken to a physician who told the parents that the child had kidney trouble. At no time was any abnormality of urine or urination noted.

Physical examination showed an extremely edematous child with the face so puffy that, without special effort to open them, the eyes remained closed. There was marked pitting edema of the extremities. The eye grounds appeared to be normal. A small, firm node was palpable behind the left ear. The lungs were clear. The heart was normal. The blood pressure was 128/80, and the remainder of the examination was negative.

The temperature was 100°F., the pulse 110. The respirations were 25.

The urine had a muddy appearance and its specific gravity was 1.025. Quantitative estimation showed approximately 3 gm. of albumin per liter of urine. The sediment contained occasional red blood cells, white blood cells, and a few hyaline and granular casts. The guaiac test on the urine was positive. The blood showed a red cell count of 4,900,000, with a hemoglobin of 70 per cent. The white cell count was 11,350, 67 cent polymorphonuclears. A phenolsulfonphthalein test showed 40 per cent excretion of dye. The serum cholesterol was 685 mg. per cent and the serum protein 3.9 gm. per cent. The chlorides were equivalent to 103 cc. N/10 sodium chloride. A throat culture was negative. A blood Hinton test was negative. Tuberculin tests were negative. The basal metabolic rate was +4 per cent for weight and +10 for height.

X-ray examination of the chest showed the diaphragm high in position, particularly on the left side. There was normal respiratory movement. The heart was transverse in position, and the lung fields were clear. A plain film of the abdomen showed findings consistent with fluid in the abdominal cavity. A film of the sinuses exhibited thickening of the mucous membrane of both antrums, with questionable fluid in the right antrum. The mucous membrane of the ethmoid cells was thickened, and the frontal sinuses were not developed.

The patient's general condition did not change very much throughout his hospital stay, except for the evident development of ascites during the first week. The temperature fluctuated between 98° and 100°F., and the urine remained essentially unchanged, although the amounts of albumin excreted varied between 3 and 15 gm. per liter. The plasma cholesterol gradually rose to 835 mg. per cent, but the nonprotein nitrogen never rose above 33 mg. per cent. The serum protein fluctuated between 3.7 and 4.5 gm. The edema, which subsided following entry, recurred during the third hospital week. On the twenty-fourth hospital day the temperature suddenly rose to 105°F. Friction rubs were heard on both sides of the chest, abdominal pain developed and the abdomen became very tender and spastic. His condition became rapidly worse, and he died on the twenty-seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ALLAN M. BUTLER*: To begin with we have a boy who is 5 years old and therefore is neither too young to have hemorrhagic nephritis nor too old to have some kind of congenital anomaly of his kidneys or urinary tract which might have predisposed him to renal disease. No mention is made of any deficiency in his diet and his heart was normal, so that the edema which was the patient's presenting symptom was neither of a deficiency nor cardiac origin. Therefore, I think it

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is fair to say that the edema was based on some renal disease and that the question before us is to decide what type of renal disease.

The history indicates an insidious onset with no preceding acute infection. This is against an acute hemorrhagic nephritis which has very quickly passed into a progressive form and entered into a nephrotic stage. Such a progression of an acute hemorrhagic nephritis may occur in children, but occurs only rarely, as approximately 95 per cent of children with acute hemorrhagic nephritis recover from their initial attack rather promptly. In contradistinction to ordinary hemorrhagic nephritis, Aldrich, of Chicago, and Lyttle, of New York, feel there is a progressive type of glomerular nephritis that is almost specifically characterized by its insidious onset, and this type of nephritis has a high mortality. Nephrosis is also characterized by an insidious onset. The history, therefore, is consistent with either this latter type of glomerular nephritis or nephrosis. Many people believe that a distinction between the two conditions at a postmortem examination is a rather academic question. But the clinician dealing with a patient who is still living finds it a distinction which is well worth his attention. In chronic glomerular nephritis the mortality is nearly 100 per cent. In nephrosis the prognosis is good except for the patient's susceptibility to peritonitis or other overwhelming infection, as a result of which the mortality is approximately 50 per cent. This difference in prognosis modifies our attitude in the treatment of these two types of patients and therefore makes a differential diagnosis more important than the mere answering of an academic question.

In general, the story of this patient is that of nephrosis, but there are three points that are out of line for a typical nephrosis. First, the blood pressure of 128/80 is too high. We are given only one reading and we wonder whether that was taken on admission. Admission blood pressures are usually higher than blood pressures taken later after the patient has become accustomed to having the blood pressure measured. Unless the blood pressure was taken repeatedly and found to be consistently elevated, I do not think we need pay much attention to it. Secondly, the patient is reported to have had red cells in the urine, and the urine is described as "muddy." I am not sure just what that means. Does the patient have such a number of red cells in the urine as to be characteristic of glomerular nephritis or has he only such a number as might occur in the highly concentrated urine of a nephrotic patient? The normal patient has red cells in a fresh, acid, concentrated urine. Addis has given a technic for examining the urine sediment for the differential diagnosis of chronic nephritis and nephrosis. Without such careful examination of the urine sediment an interpretation of the findings is difficult. This patient was probably oliguric, voiding two to three times a day. The specific gravity of the urine was 1.025 at a time when there was only 3 gm. of albumin per liter, and this small amount of albumin would not demand any appreciable correction in the specific gravity, which incidentally means that the renal function is too good to be suggestive of chronic glomerular nephritis. We therefore, do not need to place great importance on the red cells in the urine. In appraising the urine sediment one would also like to know whether the urine was acid or alkaline, for in an alkaline urine that has remained in the bladder for some time red cells and cellular casts may be largely dissolved. A description of the urinary casts would also be helpful in this differential diagnosis. The third point is the slight amount of albumin that this patient excreted in the urine. The patient with nephrosis usually has far more than the quantity mentioned here unless he is in a phase of remission with increasing serum protein concentration and the disappearance of edema.

The low serum protein explains the edema. One might wonder whether the serum protein increased with the subsidence of the edema following entry, or whether the reported increase was due to the fact that the proteins were determined by the refractometer method and the increase merely reflected the increase in plasma cholesterol. The nonprotein nitrogen is reported as never going above 33 mg. per cent, even in the later stage of the patient's illness. This again indicates a relatively good kidney function because we can be fairly sure that the patient had a scanty urine volume. The phthalein excretion also indicates good kidney function. We may comment in passing on the fact that we have a patient with a blood cholesterol of 700 mg. per cent and a normal basal metabolic rate, so that the plasma cholesterol and metabolic rate do not show an inverse ratio. Perhaps the metabolic rate should be viewed with some skepticism for one wonders what the standard of reference was in this edematous patient.

The x-ray pictures are explained by gas in the stomach and small intestines and by the ascites. An edematous patient with a low serum protein and ascites usually has an edema of the wall of the intestine and with this a tendency for the accumulation of gas. This at times becomes very distressing and interferes with eating, thus complicating therapy. Toward the end of the patient's illness one wonders whether a blood culture was taken and, if so, whether it was positive.

At necropsy this patient must have had generalized subcutaneous edema. He probably did not have a sinusitis in spite of the x-rays showing clouding of the antrums. The thickening of the mucous membranes of the antrums and ethmoid

cells was merely part of the patient's generalized edema. I believe that he had a fibrinous pleurisy with some free fluid in the pleural cavity. The bilateral friction rub makes one wonder how high or how low it was. If it was high it is indicative of a pleurisy, which is quite natural, as drainage of the infected peritoneal cavity would be through the diaphragm. If, on the other hand, the rub was low, it might have been a rub over the liver and spleen coincident to the peritonitis. The liver should have been found to show slight atrophy and degeneration of the parenchymal cells, particularly around the central areas of the lobules. There may have been some acute reaction in the liver as the result of the terminal infection. It is usually risky to guess about the pathology of kidneys for one may frequently be very wrong. In this case we should guess that the kidneys were the large and edematous kidneys characteristically seen in lipoid nephrosis. There should be some cellular infiltration in the glomerular tufts. Here and there may well have been a little scarring of the glomeruli or beginning crescent formation in the capsules. But such glomerular lesions can probably be accounted for on the basis of the terminal infection and the degree of pathologic involvement of the tubules. The tubules should show the typical changes of epithelial degeneration described so adequately by Addis and Oliver and by Blackfan and Wolbach in what the former call degenerative Bright's disease and the latter call acute tubular nephritis but is more commonly known as lipoid nephrosis.

Dr. Richard S. Eustis: I would like to ask Dr. Butler what he thinks the etiology is. How much weight does he put on the pansinusitis?

Dr. Butler: Without examining the mucous membranes of the sinuses one cannot tell whether a sinusitis is present in such edematous patients. I would assume that he did not have a sinusitis but merely had edema of the membranes. As to the cause of death, I would assume on the basis of chance and because of the fibrinous character of the pleural exudate as revealed by the friction rub that the patient died of a pneumococcus peritonitis.

Dr. Eustis: I was referring to the etiology of the nephritis.

Dr. Butler: Various people have tried to learn the etiology of nephrosis, and to my knowledge no one has had success. Similarly, we do not know the etiology of the hemorrhagic glomerular nephritis that has an insidious onset. Longcope has endeavored with some degree of success to associate ordinary glomerular nephritis with a streptococcus. To say it is the result of an allergic reaction is not too enlightening.

A Physician: I would like to ask if the blood cholesterol goes higher in children than in adults. This is tremendously high. We have never seen such a figure in adults.

Dr. Butler: In my experience plasma cholesterol in adults may be as high as reported here.

Dr. Siegfried Thannhauser: I would like to call your attention to a kind of nephrosis that I have seen and have found described in the literature in Germany. It is a kind that develops at the same time as portal thrombosis and renal thrombosis but without clinical signs of thrombosis. The picture is generally the same as the picture of thrombosis of the renal vein. It is difficult to differentiate this picture and the real picture of nephrosis if there is not a vein which actually is thrombosed. This condition is very rare.

Clinical Diagnoses

Nephrosis.
Acute hemorrhagic nephritis.

Dr. Allan M. Butler's Diagnoses

Degenerative Bright's disease—lipoid nephrosis with secondary glomerular lesions.
Generalized subcutaneous edema.
Edema of mucous membranes of sinuses.
Fibrinous pleurisy.
Ascites.
Pneumococcus peritonitis.
Atrophy and degeneration of parenchymal liver cells.

Anatomic Diagnoses

Acute nephrosis.
Subacute glomerular nephritis, slight.
Primary pneumococcus peritonitis.
Acute pneumococcus pleuritis.
Bronchopneumonia.
Acute atherosclerosis.

Pathological Discussion

Dr. Tracy B. Mallory: The autopsy in this child showed a very much enlarged pair of kidneys, two or three times the normal size, which were, as predicted, pale and edematous. The capsules stripped back very easily, almost of their own accord. Microscopically the kidneys showed significant changes in both the glomeruli and the tubules. In the glomeruli there was a distinct proliferation of the endothelial cells lining the capillaries, but there was no capsular proliferation or crescent formation. Once in a while in the capsular space about a glomerular tuft one would see a red cell and not infrequently one would find a tubule packed with red cells. On the other hand these changes were all minimal in character. If you looked carefully over the sections you would find

that nearly every glomerulus showed some change, yet every glomerulus had many patent capillary loops, and, looked at from the morphologic point of view, appeared as if it should have been a reasonably efficient filter. The tubules, in contrast, showed much more marked changes. With a fat stain moderate fat deposits were present but not nearly so much as I have seen in a number of cases of lipoid nephrosis. Rather more striking was the acute degeneration of the tubules, with desquamation of lining cells and a quite remarkable number of mitotic figures in the persisting epithelium. It was not unusual to find a cross section of a single tubule showing three mitotic figures in a total of a dozen cells. To sum up, we have widespread but not severe or very acute changes in the glomeruli, and very striking evidence of acute degenerative changes in the tubules.

I think that classification is just about as difficult at this stage of the game as it was before the postmortem. The purist would probably refuse to admit it as a true nephrosis, and yet I cannot help being impressed with the fact that by all odds the major changes seem to be in the tubules rather than in the glomeruli. Despite the glomerular lesions I prefer to classify the case with the degenerative rather than the inflammatory type—a nephrosis rather than a nephritis.

The heart was not hypertrophied. On the aortic valve and all along the aorta were rather more atheromatous plaques than we would expect to see in a child of 5. Many people do not realize that children frequently have atheromatous plaques, and it is not surprising to see a few. This child had more, however, than one could possibly accept as normal.

The terminal infection, as it so frequently is in these cases, was a pneumococcus infection due to primary peritonitis. There was no lesion of any of the viscera to account for the peritonitis. He also had bilateral pleuritis and a little bronchopneumonia.

Dr. Eustis: Was there a sinusitis?

Dr. Mallory: We did not have permission to examine the head; I cannot answer that.

CASE 23292

Presentation of Case

A 20-year-old American salesgirl was admitted complaining of difficulty in walking.

About 6 years before entry the patient developed a slight limp resulting from an ill-defined discomfort in the right hip. X-rays were said to be negative for scoliosis. The limp recurred intermittently and occasioned no great inconvenience until 2½ months before coming to the hospital. At that time while working quite hard during the Christmas rush, she developed considerable pain in the right hip and in the lower back, which was aggravated by walking and relieved by lying down. Since that time the symptoms had become progressively worse, and 3 weeks before entry she was compelled to discontinue work.

Physical examination showed a moderately undernourished young girl in no acute discomfort. The tonsils were slightly reddened and cryptic. There was marked right dorsal and left lumbar scoliosis, the apex of the dorsal curve being between the eighth and ninth thoracic vertebrae. There was slight lumbar lordosis, and marked tenderness was elicited over the entire upper half of the sacrum. Forward bending of the trunk was limited to 25° and there was considerable limitation of all other movements of the lumbar spine. Deformity of the thorax corresponded with the scoliosis. The right lower extremity exhibited a 2.5 cm. atrophy of the right thigh and a 3.5 cm. atrophy of the calf. There was no shortening. There was limitation of adduction and external rotation of the right hip. Forced flexion of the thighs produced considerable pain in the lower lumbar region. There were weakness and atrophy of the right gluteal muscles and an area of sensory anesthesia in the distribution of the right second and third sacral nerves. The right ankle and knee jerks were absent. The character of the patient's limp was described as being of the right gluteus maximus type. The remainder of the physical examination was negative.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. The blood showed a red cell count of 4,900,000, with a hemoglobin of 90 per cent. The white cell count was 14,000, 70 per cent polymorphonuclears. The serum phosphorus was 3.84 mg. per cent, the serum calcium 10.9 mg. per cent, and the serum protein 6.4 gm. per cent. A blood Hinton test was negative. A lumbar puncture between the second and third lumbar vertebrae showed an initial pressure of 55 mm. of water, with normal dynamics. The total protein of the fluid was 75 mg. per cent, and a colloidal gold curve was 0012333210. The spinal fluid Wassermann was negative.

An x-ray of the spine showed a large globular defect involving the fifth lumbar vertebra and the upper half of the sacrum. In the center of this area the bony tissue of the sacrum had completely disappeared. In another area there were fine, thin layers of bone remaining on the surface. This was particularly true in the left lateral as well as the upper aspect of the lesion. There was no evidence of new bone formation. There was slight tilting of the pelvis to the left. Two days later an x-ray of the pelvis showed, in

addition to the previous findings, a fracture line running through the small portion of the upper bodies of the sacrum, which had not yet been destroyed. A barium enema passed freely around to the cecum. There was no evidence of obstruction. The sigmoid and lower descending colon were displaced anteriorly, apparently by a pelvic mass. The films showed a curved defect in the lower sigmoidal region such as might be produced by pressure from an extrinsic mass.

A week after entry another lumbar puncture showed a spinal fluid protein of 111 mg. per cent. On the eighteenth hospital day an x-ray of the spine after the introduction of lipiodol showed that the lipiodol failed to reach the terminal sac of the dorsal space and formed a cap within the region of the fifth lumbar vertebra. Shortly afterward an operation was performed.

Differential Diagnosis

Dr. W. Jason Mixter: This patient has had some trouble over a long period of time—trouble of sufficient severity so that she had x-rays taken during the early part of her illness. The x-rays were said to be negative for scoliosis. We have never seen them, and we do not know anything more about them. If she showed no scoliosis at that time it is probable that she showed no gross lesion of the pelvis or spine by x-ray.

We have a very definite increase in symptomatology during the last few weeks before she entered the hospital, but no real change in the character of her symptoms except that she was having more pain and that she was relieved by lying down and made worse by moving about. There is nothing very much that we can go on so far, except that this was a chronic lesion, presumably somewhere below the dorsal vertebrae. We cannot tell whether it was a bony lesion, whether it was a neurologic lesion, or whether it was something in the pelvis itself.

Scoliosis of this type, coming on in adult life, usually is evidence of definite disease of the spine or cord and is not like the scoliosis of childhood where one does not find a definite lesion.

"There were weakness and atrophy of the right gluteal muscles and an area of sensory anesthesia in the distribution of the right second and third sacral nerves." She had definite atrophy. That is really the first definite thing we have in the way of a sign. Where we have as much atrophy as that we have to consider interference with nerves or nerve roots somewhere. I think we might have as much atrophy as that as the result of bone disuse, but I should hardly expect it in a young woman who had only been compelled to discontinue her work for 3 weeks.

"The right ankle and knee jerks were absent." There again we have a suggestion of a definite nerve or nerve root lesion, but it is not a positive sign. We may get absence of reflexes in conditions that are far different from a true nerve lesion. I saw a patient yesterday who had an absent ankle jerk and markedly weak knee jerk and who had osteomyelitis of the lower end of the femur. Just what the mechanism is, I do not know.

"The character of the patient's limp was described as being of the right gluteus maximus type." I should like to ask the orthopedic department what that means. I do not know.

Dr. Sumner Roberts: It is slight listing to the side and partially to the back. It is sometimes hard to differentiate the medius and the maximus.

Dr. Mixter: The polymorphonuclears are a little high. With that white count one would have to consider whether this may be some kind of inflammatory lesion.

The lumbar puncture showed a low initial pressure, but that means nothing so long as the dynamics were normal. With that much protein in the spinal fluid and the change in the colloidal gold curve we have to consider very definitely a lesion within the spinal canal, and by the spinal canal I mean the whole length down into the sacrum. We know that we can have increase in protein above a lesion in the spinal canal, although it is not so marked as the increase in protein below the lesion. This apparently was above the lesion, because there was no interference with the dynamics. Of course there are certain lesions of the spinal canal that will increase the total protein with no change in dynamics below the lesion on account of the fact that the lesion is very small.

May we see the x-ray?

The lower end of the spinal canal is like the grab bag at the county fair. One can find almost anything in it. There may be all kinds of tumors, both primary and metastatic, and also congenital defects without tumor formation. The variety of lesions is very large.

This is a very good plate. It shows the tremendous globular defect, with the vertebrae perfectly good above it, and the lower part of the sacrum below, which looks normal. The defect runs far out on both sides and seems to be smooth. There is no evidence of new bone formation. First we have to try to rule out certain things. If this were a spina bifida, we should expect to see the laminal stumps on the side and the vertebrae immediately above would be affected. I think that we can rule it out. More than that, if she had spina bifida, it would have been mentioned at the time of the previous x-ray. We cannot be sure of that, but it is probable. This does not look like

a lesion originating anywhere in the bones of the pelvis, such as sarcoma or anything of that sort; and I should say that it does not look like tuberculosis. I should think there was something in the spinal canal which had spread the whole sacral canal wide open—simply ballooned the whole thing right out.

We have enough information from the x-ray findings and the neurologic examination to let us make certain generalizations. In the first place, we have something which invades the spinal canal and causes a certain amount of nerve root damage, which has forced the bony structures about the spinal canal widely apart, and I should say that presumably the mass was either within or very close to the spinal canal and involving it. We can have any kind of tumor in the lower end of the spinal canal, and I should say that this was some kind of new growth, either congenital or coming on at a later date. We can have various tumors of the sacrum. One of the things that we know is common in this region and that causes a rather large tumor is a chordoma. I want to ask Dr. Hampton a question. We have been trying to read the x-ray films and perhaps our interpretation was wrong.

Dr. Aubrey O. Hampton: The notes as given in the history are quite complete.

Dr. Mixter: I want to know whether the defect goes through the sacrum to the front.

Dr. Hampton: I had hoped you would not ask that. We have bone trabeculae crossing it in the upper left portion, but none on the right side. Then this pressure defect on the sigmoid is some evidence that the mass has extended into the pelvis. My argument, before I found out what this was, was that the pressure defect could be produced by the acute lumbar sacral curve.

Dr. Mixter: I thought that we could see the anterior wall.

Dr. Hampton: Yes; on one side, but I do not think you can say that there is much bone on the right side. I think that it probably is destroyed here. On the x-ray findings we cannot rule out a chordoma. However, I do not think that it looks like a chordoma.

Dr. Mixter: I do not see how it could be an anterior spina bifida without destruction posteriorly and without more evidence. I will stick to it that it is not a spina bifida. I am neglecting the fracture which is shown by x-ray, because it is simply an accidental finding, and has nothing to do with the original lesion. The bone was so weak that she developed a spontaneous fracture, and that we do not care much about.

"On the eighteenth hospital day an x-ray of the spine after the introduction of lipiodol showed that the lipiodol failed to reach the terminal sac of the dorsal space and formed a cap within the region of the fifth lumbar vertebra." In other words there was a mass filling this defect. I am not sure what chordomas show with lipiodol injection, but I do not believe they show such cap formation. Therefore, I am going back to a tumor of the cauda equina. Whether it is some kind of congenital lesion—cyst, lipoma or something of that sort—or whether it is a tumor originating from one of the nerve roots or from the filum terminale, I do not know. I do not believe we can go much farther than that in diagnosis. I should say that it probably originated from the filum terminale, and of such tumors, the ependymoma is commonest.

Dr. Tracy B. Mallory: What would you have done had the case been yours, Dr. Mixter?

Dr. Mixter: I would have explored the mass, probably beginning above it, in the normal spinal canal, and then followed it down to see what could be found.

Dr. Hampton: Would you have put lipiodol in?

Dr. Mixter: Yes; I think so, but I would not have been very insistent about it one way or the other.

Dr. Mallory: Dr. White, you saw this patient, have you anything to add?

Dr. James C. White: Nothing, except that I did a rectal examination and thought I could feel a definite mass, pushing the rectum forward.

Dr. Hampton: The x-ray department had quite a time trying to make the diagnosis. My first impression was that it was too smooth for a malignant tumor but then when we discovered that the patient actually had a mass in the pelvis by rectal examination, and that the sigmoid was displaced, we weakened and yet insisted that lipiodol be put in to rule out various congenital defects such as spina bifida.

You could not do much for a spina bifida of that type could you, Dr. Mixter?

Dr. Mixter: No, except that a defect like that with spina bifida would almost surely suggest an associated tumor—a lipoma or a dermoid.

Dr. Hampton: I remembered that you told me that, and that was another reason for putting lipiodol in.

Dr. White: Dr. Adson reported a case of chordoma from the Mayo Clinic with an x-ray picture almost identical with this.

Dr. Hampton: The chordomas that we have seen have not been smooth tumors; they are irregular in outline as are other malignant tumors.

Preoperative Diagnosis

Chordoma.

Dr. W. Jason Mixter's Diagnosis

Tumor of the cauda equina (ependymoma ?).

Anatomic Diagnosis

Ependymal glioma.

Pathological Discussion

Dr. Tracy B. Mallory: Dr. Mixter has gone as far as one could go without exploration and biopsy of the tumor, which were done in this case. A very soft, almost jelly-like tumor was found occupying much of the sacrum and invading a small portion of the ilium. Dr. Cave did a biopsy, and it showed a typical ependymal glioma. The gliomas which occur in this region are very apt to be of the so-called ependymal type, in which the cells appear almost epithelial in character but do have demonstrable glial fibrils and "sucker feet" running down to the blood vessels, which permit one to establish them definitely as gliomas.

The outlook of the case is hopeless, I presume. It was impossible to resect the tumor, which from the operative findings was obviously invasive, and it is not a tumor that is apt to prove radiosensitive.

Dr. Mixter: There is this to be said. A tumor of this sort is soft and gelatinous. One might be able to scrape out a good deal of it and carry the patient over a considerable period of time. Do you know why that was not carried out?

Dr. White: She had a trophic ulcer.

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HOW MANY SECTION MEETINGS ARE DESIRABLE FOR OUR ANNUAL MEETINGS?

One of the many matters of interest considered at the annual meeting of the Massachusetts Medical Society was whether there should be more or fewer sections. The function of a section is to provide a meeting for the consideration of a special department of medical practice.

This question was brought before the Council in a petition to separate the subjects of radiology and physical therapy, now combined, and thereby make a separate section for each of these departments of practice. This request was denied after the argument was advanced that under existing conditions it seems best to avoid having especially important subjects discussed in separate rooms synchronously. This conflict has imposed the responsibility of weighing the value of one section meeting against that of another, which has led at times to a feeling of disappointment.

The unofficial announcement of the unanimous vote of the members of the Section of Tuberculosis to surrender its organization with the advice to have this subject incorporated into the Section of Medicine evidently met the approval of the Council. The success of the well-arranged "combined clinical meeting" with its large attendance seemed to indicate approval of this type of meeting for the annual convention. The very excellent work carried on by the several hospitals was well presented by recognized leaders in the several fields of practice, and the general practitioners were given up-to-date information of standardized forms of treatment. In this meeting specialists presented a symposium of progress in medicine. Every desirable feature of a special section meeting was met.

The attendance at the annual meeting was about 20 per cent of the membership of the society, and we are quite sure that the majority of those present was made up of doctors doing more or less general practice. As one studies the programs of other annual meetings and even that of the American Medical Association, it seems quite evident that the great majority of the papers presented deal with subjects which properly are included in the two major departments—medicine in its general acceptance of the term and surgery. This leads to a question of the advisability of having an annual session of the Massachusetts Medical Society allocate all of its scientific papers and discussions to combined medical and surgical programs which will cover the time given to scientific exercises. This would not include the Shattuck Lecture, a prominent and separate feature of our annual meetings.

We hope that no person who has planned a section meeting will assume that any criticism of such meetings or the contributors thereto is intended. There is no ground for any expression of this sort, and if the suggested changes are adopted, the specialists who conduct the exercises will have larger audiences than under the previous plan and the attending physician will have a larger acquaintance with available persons who may be of service in those times of uncertainty which are frequent in the daily routine of practice.

There may be other suggestions respecting the annual meetings of our Society which will, we hope, be published in our columns and which will, we are sure, be considered by the officers in charge of the programs.

HYPERSENSITIVENESS TO COLD

The studies of Horton and Roth of the Mayo Clinic on individual hypersensitiveness to cold have received considerable attention and have already been commented on editorially in the *Journal of the American Medical Association* (**108**: 1975 [June 5] 1937). The implications, however, are so important, in view of the fact that in Minnesota alone some 3,000 persons since 1920 have been drowned while swimming, that a review of the conditions seems justified, particularly at this season of the year.

The theory offered by these investigators is that physical agents, such as cold, probably cause increased permeability of the tissue cells and permit the release of chemical substances. Apparently one of these is a histamine-like substance which, in addition to producing the usual urticarial changes locally, frequently attains sufficient concentration in the general circulation to produce reactions comparable to those obtained when histamine is injected. It is quite probable that many of the deaths attributed to cramps suffered while an individual is swimming may actually be due to this reaction.

Hypersensitiveness of the individual to cold may be determined by immersion of the hand in ice water for five minutes. If swelling of the hand occurs after it has been removed from the water, the patient is presumably hypersensitive. A drop in blood pressure, an increase in pulse rate and flushing of the face indicate a systemic reaction. Individuals who exhibit a systemic reaction, according to Horton and Roth, are likely to show symptoms of collapse if they swim in cold water.

Hypersensitive persons, however, may be desensitized either by short immersions of the hands in cold water for one or two minutes twice a day for three or four weeks, or by subcutaneous injections of 0.1 mg. or less of histamine twice a day for two or three weeks.

THE OCTOPUS

The family doctor whose patients have been insidiously and progressively diverted to the offices of specialists must have conflicting emotions about the value of scientific medicine. Specialization is the mechanism of science; the specialist is merely the temporary and replaceable operator of the machine. It is not the specialist but scientific medicine that has tended to take over the direction of so many ailing, or at least complaining, individuals.

The ability of the bacteriologist to recognize, then cure and prevent diphtheria; the surgical removal of diseased organs which previously were considered fatal; the control and elimination of what were formerly reservoirs of infection, all these are surely comforting changes for the family doctor to look back upon. So far as they are the result of any influence, they are due to that of scientific medicine. Science has, on the other hand, left great gaps in the medical fabric with which the family doctor was so familiar. These lost values are largely emotional ones, but science is slowly learning that the world is turned by emotion as well as motion. Like most lost values they have customarily been indicated in a sentimental way. That they nevertheless exist as deficiencies in the science of medical care has become apparent through the sincere concern recently expressed by some of the leading scientists themselves.

What is being called the "social component" of medicine, however, is developing in the true scientific manner: observation; analysis; research; the experimental method. One suspects that they may be the only approaches known by the scientific physician. Whether lost sympathies are going to respond to this objective treatment is an interesting speculation. If they do, the scientific method as applied to medical care may engulf another large field of medical effort, and if it does, what will become of those dissenters who have continued to talk of the art of medicine? Those who merely talk are easily disposed of; as spellbinders they will move on to other fields and continue to talk, and in a small way to practice their quaint methods of education, of healing, and of worship Human nature being what it is, they will be sure to have a following, for there are always those who are sure the world is wrong.

The world's chief concern, however, is not with those who like to talk, but with the many who have for so many years *practiced* the art of medicine. What is to become of them if the octopus continues to reach for their precious bread and butter? The answer is plain. Men and women who do not chant about the good old days are appearing in our communities in increasing numbers. You see them at meetings where scientific medicine, nursing and public health are discussed. You find them taking blood cultures and doing renal function tests in their patients' homes. You see their patients gladly following them to hospitals when these modern havens provide the safest

refuge. They are employed and appreciated and paid by the people who are doing the work of the world. If they were more in the habit of emotional breakdowns, you would hear them glory in their sacrifices for the "less fortunate," but they are generally too occupied to indulge in this social vanity. These are the general practitioners of today, who are supplying the every need that practitioners ever supplied by virtue of their willingness and ability to incorporate the methods of the octopus into the practice of the art of medicine.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

M. Fletcher Eades, M.D., *Secretary,*
19 Bay State Road,
Boston, Mass.

Case History No. 29. Bleeding at Five Months

While driving an automobile on March 7, 1936, Mrs. D., a white, American housewife, 32 years of age, began to flow very freely. She was about 5 months pregnant.

Her family history was essentially negative. Her mother died at 70 of a heart ailment. Her father was living and well. She had one brother and sister, alive and well. There was no history of tuberculosis, diabetes, malignancy or hemorrhagic disease.

The patient had had pneumonia, whooping cough, chickenpox and measles. Her tonsils had been removed and her nose operated on for a sinus infection. Six years ago she had been treated for duodenal hemorrhage, without operation. Her periods had begun at 13 years, were always regular, of the 28-day variety, lasting 6 days. Her last period was October 13, which would normally make her due about July 20.

She was a well-developed and nourished woman. The breasts were enlarged and firm, and Montgomery's glands prominent. Her heart was not enlarged, and there were no murmurs. The lungs were resonant throughout, and there were no rales. The extremities were normal. There was no glandular enlargement. Her blood pressure was 130/60.

The blood Wassermann was negative. Her urine showed no abnormalities. The hemoglobin was 80 per cent, and the red blood cell count 4,200,000.

A series of selected case histories by members of the section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the section.

She had been seen routinely in the office three times before the onset of bleeding. Her weight had shown a normal increase, but the uterus, between the visit on February 14 and March 6 had risen 4 cm., suggesting a somewhat abnormal increase.

The patient was taken immediately to the hospital and, when seen directly upon entrance, was definitely in labor. She was flowing moderately, and had flowed considerably by the appearance of her clothing. As her hemoglobin and red count were relatively high, there had not been an abnormal amount of hemorrhage. Since the patient was in labor and actually bleeding, examination was made to diagnose the cause of hemorrhage. A rectal examination was done and was entirely unsatisfactory. Vaginal examination showed the entire sac of membranes filling the vagina. This led to the supposition that the cervix was fully dilated. The membranes were ruptured artificially with the escape of a large amount of fluid, enough to characterize the condition as hydramnios. A moderate amount of fresh blood and some clots came away. A vaginal examination was then made to determine the presenting part, but none was felt in the vagina. The cervix was high in the vault and dilated not more than two to three fingers. When the fingers were put through the cervix, the placenta was definitely encountered. The condition was a partial placenta praevia, with separation and accompanying hydramnios. The baby was delivered by version, and because of the small degree of dilatation, the head was crushed. The placenta was manually removed after the birth of the baby; there was no bleeding after delivery. The patient made a perfectly normal convalescence and was discharged at the end of 10 days.

Comment. The handling of this case is open to considerable criticism, in spite of the normal convalescence. When it was found that the cervix was only two to three fingers dilated, it would have been much more conservative to have packed the cervix tightly with gauze and allowed nature to complete the dilatation; or to have employed slow extraction, using the Braxton Hicks' maneuver; or even to have used a bag. At 5 months the amount of bleeding from the separation of the placenta, with the baby's body in the cervix and labor progressing, would have been relatively slight. The possibility of tearing the cervix would have been entirely eliminated. The risk of infection would have been reduced to a minimum. The cervix not fully dilated at any stage in pregnancy should demand conservative treatment; and the mere fact that this patient did well is no argument against conservatism.

MISCELLANY

NEW DEAN FOR MIDDLESEX UNIVERSITY SCHOOL OF MEDICINE

The trustees of Middlesex College announce the appointment of Dr. William M. Konikov, of 11 Keswick Street, Boston, as dean of the Middlesex University School of Medicine for the session beginning in September, 1937. He will succeed Dr. Frank L. Whipple, of Lynn, who will become dean emeritus and vice-president of Middlesex University.

Dr. Konikov was born in Boston and is a graduate of Harvard College and Boston University School of Medicine. He was a student for a year at Friedrich-Wilhelms University, Berlin, in the field of anatomy. He interned at the Massachusetts Memorial Hospitals for two years, and served a third year as a resident in the department of urology. In 1932 he became a member of the staff of the Massachusetts Memorial Hospitals and of the medical faculty of Boston University School of Medicine, where he was assistant in anatomy for three years, and subsequently in genito-urinary surgery. He severed these connections, when he was appointed professor of anatomy at Middlesex in September, 1936.

Dr. Konikov is a member of the Massachusetts Medical Society, the Neisserian Medical Society of Massachusetts, the Greater Boston Medical Society and the Massachusetts Urological Society, and a fellow of the American Medical Association.

MARYLAND ERADICATES BOVINE TUBERCULOSIS: OTHER STATES MAKE PROGRESS

Maryland is the forty-fourth state to eradicate bovine tuberculosis. It became a modified accredited area July 1, —that is, infection among cattle has been reduced to less than 0.5 per cent as shown by the tuberculin test,—the U. S. Department of Agriculture reports.

Three other states were also conspicuously successful in tuberculin-testing work during June. California reported the following counties for modified accreditation: El Dorado, Lake Sacramento and Yuba. New York officials reported the necessary progress to accredit four counties—Chenango, Delaware, Lewis and Otsego.

In South Dakota, officials in charge of tuberculosis-eradication work reported five counties—Brown, Hyde, Jerauld, Moody, and Spink—as accredited. Similar work is being conducted in Puerto Rico, where seven municipalities were placed in the modified accredited area July 1. In other states and territories tuberculin testing and retesting are likewise progressing satisfactorily, federal officials report.

CAMPAIGN AGAINST TRICHINOSIS WILL BE CARRIED TO PRODUCERS

To acquaint swine producers more fully with the need to prevent infestation of their hogs with trichinae, the U. S. Department of Agriculture is sponsoring a program of information on the subject. This activity among producers is a counterpart of a similar campaign conducted among consumers for many years to induce them to cook pork thoroughly as a safeguard against trichinosis.

In a recent circular letter, Dr. John R. Mohler, chief of the Bureau of Animal Industry, directs each inspector in charge of federal veterinary activities in the principal hog-raising states to designate a member of his force to contact farmers and other swine producers individually and in meetings for the purpose of more effective control of trichina infestation in hogs.

"These contacts," he states, "should be made as often as opportunities for doing so present themselves and should be continued over a period of several years." Dr. Mohler points out that the persistence of trichinosis in man is likely to react unfavorably sooner or later on the swine industry and injure it financially. The trichinosis educational campaign is expected to prevent such an occurrence.

The Bureau of Animal Industry's recommendations, as set forth in the official letter to inspectors, are in part as follows:

Inasmuch as investigations conducted in the Bureau have shown that the incidence of trichinae in garbage-fed hogs is much higher than that in hogs not fed on garbage, it is essential to stress that the feeding of raw garbage tends to spread trichinosis among swine. Other sources of trichinosis in swine are: (1) the feeding of offal from slaughterhouses; (2) the feeding of the contents of scrap barrels; (3) the failure to bury, burn, or otherwise dispose of hogs or other animals which die on lots and pastures and which may be eaten by hogs.

A strict adherence to the swine sanitation program, as developed by the Bureau of Animal Industry, will aid in preventing the spread of trichinae among hogs and will reduce the extent of infestation with these parasites. The sanitation system precludes the feeding of garbage, offal, kitchen scraps and other feed containing scraps of raw pork, and involves the use of clean pastures and sanitary housing. This system decreases the cost of swine production, favors the growth and development of pigs, and finishes pigs for market at 6 to 7 months of age. The system, if carried out as recommended, will reduce, if not eliminate altogether, trichinosis in swine, since it removes most of the known sources of trichinae.

RECENT DEATHS

PHIPPS—Walter Andrus Phipps, M.D., of 310 Safford Street, Wollaston, died July 14. He was in his eighty-third year.

Dr. Phipps attended Amherst College, and graduated from the Harvard Medical School in 1878. He was a retired member of the Massachusetts Medical Society.

His widow, Mrs. Anna C. Phipps, two sons, Rowland and Marcus, and a daughter, M. Avis Phipps, survive him.

HUBBELL—Adelbert M. Hubbell, M.D., died at his home in Haverhill on July 3. He was in his seventy-third year.

Dr. Hubbell was born in Enosburg, Vt., in 1863, the son of Oscar and Charlotte Amanda (Spears) Hubbell. He attended Phillips Academy in Andover and received his M.D. degree from Boston University School of Medicine in 1889.

Dr. Hubbell was a member of the American Medical Association, Massachusetts Homeopathic Medical Society, American Institute of Homeopathy, Massachusetts Medical Society, and the Haverhill Medical Club.

NOTICES

ANNOUNCEMENT

Kenneth A. Brown, M.D., announces the opening of an office at 482 Beacon Street, Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination and review of case histories of Group B applicants by the American Board of Obstetrics and Gynecology will be held in various cities in the United States and Canada on Saturday, November 6, 1937.

The next general examination for all candidates (Groups A and B) will be held in San Francisco, Cal., on June 13 and 14, 1938, immediately prior to the American Medical Association meeting.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania. Applications for these examinations must be filed in the secretary's office not later than sixty days prior to the scheduled dates of examination.

CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Orthopedic Consultant
Salem	August 2	Harold C. Bean
Haverhill	August 4	Arthur T. Legg
Lowell	August 6	Albert H. Brewster
Gardner	August 10	Mark H. Rogers
Brockton	August 12	George W. Van Gorder
Pittsfield	August 16	Francis A. Slowick
Springfield	August 18	Garry deN. Hough, Jr.
Worcester	August 20	John W. O'Meara
Fall River	August 23	Eugene A. McCarthy
Hyannis	August 24	Paul L. Norton

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, July 26

Saturday, July 31—

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Robert T. Monroe.

*Open to the medical profession.

September 13-17—Fifth International Congress of Radiology. Page 709, issue of April 22.

October 1 and 2—New England Surgical Society. Providence, R. I.

October 5-8—American Public Health Association meeting. New York City.

October 9—American Board of Ophthalmology, Chicago. Page 722, issue of April 22.

October 19, 20, 21—Academy of Physical Medicine. Page 723, issue of April 22.

October 25-29—American College of Surgeons. Chicago, Illinois.

November 1-12—1937 Graduate Fortnight of the New York Academy of Medicine. Page 1000, issue of June 3.

November 6—American Board of Obstetrics and Gynecology. Notice above.

April 4-8, 1938—The American College of Physicians. Page 41, issue of July 1.

June 13 and 14, 1938—American Board of Obstetrics and Gynecology. Notice above.

REPORTS OF MEETINGS

TUFTS ALUMNI ASSOCIATION

The annual Alumni Lecture was delivered by Dr. Louise Eisenhardt of the Class of 1925 at Tufts College Medical School on Tuesday, April 6. Her subject was "Observations upon Patients after Operations for Intracranial Tumors." Dr. Eisenhardt has been associated with Dr. Harvey Cushing, both at the Peter Bent Brigham Hospital and at the Yale University School of Medicine and is director of the Brain Tumor Registry.

One of the purposes of the Registry is to follow closely the progress of all patients who have been treated for intracranial tumors. The results are judged not so much by the duration of life as by the relative activity of the patient and his ability to support himself. On the basis of 2,000 complete records covering a period of 30 years, the Registry has supplied valuable information concerning the prognosis in the various types of intracranial tumors.

Dr. Eisenhardt called attention to the increasing frequency of brain tumors, attributing this to recognition of the condition by practitioners. Unfortunately, some physicians still believe that the possibility of a cure in any case of brain tumor is very remote, and therefore neglect proper treatment. It is true that the symptoms are often confusing, and that the classic signs of headache, choked disks, vomiting and impairment of vision may be absent. The growth of many tumors is slow, with a gradual development of symptoms. Often irritability or other mental symptoms are the only evidence of the disease. Only those closely associated with the patient can detect obscure changes in personality. For these reasons it is not surprising that so many victims have either been confined in mental institutions or treated for cerebral arteriosclerosis or syphilis of the central nervous system. Tumors involving the frontal lobes either by compression or by actual invasion are prone to cause these mental disturbances. The family doctor is often in the best position to notice a gradual progression of symptoms.

Glial tumors show wide variations in prognosis. The following table records the longest period of postoperative survival in the Registry:

Astrocytoma (cerebellar)	29 years
Astrocytoma (cerebral)	22 "
Spongioblastoma polare	16 "
Oligodendroglioma	13 "
Astroblastoma	13 "
Ependymoma	11 "
Medulloblastoma	8 "
Glioblastoma multiforme	4 "

The astrocytoma is the cerebellar tumor commonest in children. The patient may or may not present an advanced clinical syndrome. Sometimes unexplained vomiting is the only prominent symptom, yet an examination of the eye grounds reveals marked choking of the disks. Early attention to symptoms is imperative, so that the tumor may be removed before permanent damage has been done to vision or to brain tissue. These gliomas occasionally undergo cystic degeneration. Excision of the cyst wall alone is not sufficient for a permanent cure. The mural nodule within the cyst must be located and removed as well. In the past, these lesions were treated by aspiration of the cystic fluid, but the symptoms almost always recurred.

Another glial tumor that occurs in the cerebellum of children is the medulloblastoma. It presents a different microscopic picture, for it is a rapidly growing malignant tumor, and may metastasize to the spinal cord. The tumor can rarely be extirpated and the remnants must be treated by x-ray. Consequently postoperative prognosis is much less favorable than with the astrocytoma, which can be removed in toto. The longest survival after operation for medulloblastoma recorded by Dr. Eisenhardt was 8 years, as compared with 29 years in a case of astrocytoma.

The glioblastoma multiforme is the second commonest type of glioma; it occurs usually in the cerebrum of adults. It is extremely infiltrating and malignant, and the duration of life after operation is very short, averaging about 9 to 12 months, although Dr. Eisenhardt mentioned sev-

eral postoperative survivals of from 2 to 4 years. The advisability of excision of these tumors is problematic. The patients themselves, and generally their relatives, prefer operation with its short subsequent period of relief to the more distressing existence without surgical interference. Some of these patients are even enabled to return temporarily to work.

Gliomas such as spongioblastoma polare, oligodendroglioma and ependymoma represent smaller groups, though they are not uncommon. The postoperative survival periods have been well over 10 years in the cases entered in the Registry files.

One of the most interesting groups of intracranial tumors is that of the pituitary adenomas, which were brought to light by the fine work of Dr. Cushing. Through his influence the Registry has been able to assemble complete studies on an extremely large number of cases. The chromophobe adenoma is associated with signs and symptoms of hypopituitarism, such as diminished sexual function, scanty hair distribution and obesity. In males there may be a feminine contour of the body. In females cessation or irregularity of menstruation may occur. The chromophile adenoma causes symptoms resulting from excess pituitary secretion. The bones of the hands, feet and jaw enlarge to produce the picture of acromegaly in adults, and gigantism if the epiphyses have not united. X-rays of the bones may show the classic tufting of terminal phalanges. The lower jaw often protrudes so far that dental occlusion is impossible and the patient is obliged to wear artificial teeth to overcome this defect. The removal of both types of adenoma relieves the associated symptoms; many female patients have had a return of menstruation, and some have even borne children. Operation is attempted only to relieve bitemporal hemianopsia and primary optic atrophy, which may progress to complete blindness. Release of pressure from the optic tracts usually restores vision unless damage to them has been severe. In the acromegalic the soft parts of the hands and feet may shrink, but the bony changes remain. The longest period of survival for both types of adenoma after operation is over 24 years, and most patients are able to carry on a normal, active existence.

Meningiomas make up a large group of operable intracranial tumors. They may arise wherever arachnoidal villi abound, and the signs and symptoms vary according to their location. They are apt to invade bone and produce characteristic hyperostoses, which in many cases suggest the diagnosis. Recurrence is the rule if the tumor with its dural attachment is not completely removed. Vascularity of the tumor and the overlying bone and scalp presented a disturbing problem before the days of electrocoagulation. Hemostasis was achieved by the application of fresh muscle obtained from another patient. At the present time electrosurgery has greatly simplified the operation. Dr. Eisenhardt reported several 20- to 25-year cures after operation for meningiomas.

Acoustic neurinomas are fairly common intracranial new growths, and can usually be easily diagnosed. Tinnitus followed by deafness, suboccipital pain, difficulty in speech and in swallowing, involvement of the facial nerve and cerebellar symptoms point directly to a tumor of the eighth nerve. The results of operation are extremely encouraging, for the tumor is benign and can usually be radically removed. Cures as long as 28 years have been reported.

In conclusion Dr. Eisenhardt emphasized the necessity for earlier diagnosis of intracranial tumors. Through improved operative technic the life duration has been remarkedly extended, as evidenced by the case records of the Registry.

SPECIAL LECTURES IN ENDOCRINOLOGY

One of the series of Special Lectures in Endocrinology was delivered at the Harvard Medical School by Dr. F. L. Hisaw on March 9, on the subject "The Physiology of the Sex Cycle."

Dr. Hisaw stated that the estrus cycle of animals is made up of two parts: a follicular half, characterized by the growth of the graafian follicles; and a lutein half, characterized by the growth of the corpus luteum. When the animal goes into heat, the corpus luteum of the previous cycle has reached its peak of development and has involuted, while the follicles have grown to a preovulatory condition, and ovulation usually occurs soon after the onset of estrus. The corpus luteum grows following ovulation, and reaches a maximum in the mid-estrus period. The time interval between periods of heat is known as the estrus cycle, and is of different length in different animals.

The pituitary gland also shows rhythmic activity during the estrus cycle. It liberates two hormones: FSH (follicle-stimulating hormone), which acts directly on the ovarian follicles, and LH (luteinizing hormone), which causes the development of the corpus luteum. There is a correlation between the levels of these hormones and the stage of the cycle—LH being highest at the time of ovulation and FSH lowest. In the middle of the cycle, during the corpus luteum phase, there is a reversal of these relations; FSH is high and LH is low. The pituitary gland as well as the ovary is thus seen to go through a cycle.

A study of the effects of the pituitary hormones has shown that FSH causes a development of ovarian follicles to a preovulatory condition, but that there is no further development unless LH is given. During the time that the follicles are developing the corpus luteum is active, and as long as this activity continues the follicles do not progress beyond the preovulatory stage. Removal of the corpus luteum from an animal in which the follicles have been brought to a preovulatory condition results in an almost immediate onset of estrus and complete development of the follicles. The depressant action of the corpus luteum on ovarian development is further illustrated by the fact that injections of corpus luteum hormone prevent the occurrence of heat. The corpus luteum hormone is thus seen to determine to a certain extent the spacing of the estrus cycle.

The strength of FSH in the pituitary gland is greatly increased in castrate animals—an increase which is prevented if the animals are given injections of estrin, but which is not influenced by the administration of physiologic doses of corpus luteum hormone.

A possible explanation for the arrest of follicle development in the preovulatory state under continued FSH stimulation, and for the sudden increase in size immediately preceding ovulation, is afforded by a study of the LH of the pituitary. LH administered alone has no effect on the weight of the ovary, but when it is given in conjunction with FSH it produces marked enlargement of the ovaries and corpus luteum development. By grading down the amount of LH it is possible to obtain large ovaries filled with follicles in the preovulatory state, but no corpora lutea. A slight further increase in LH produces ovulation and luteinization. These findings indicate that there is a threshold for LH which must be exceeded before ovulation and luteinization occur, and suggest that the preovulatory swelling observed during heat marks the appearance of LH in physiologic amounts.

In the rat, LH appears in the preovulatory period, owing to some action of estrin on the pituitary which causes its release, but this release occurs only when the level of cor-

pus luteum hormone falls and ceases its inhibitory action. The estrin secreted by the follicles in the preovulatory development does not liberate LH from the pituitary, because of the presence of the corpus luteum hormone in relatively high concentration.

Ovulation should not be considered as a "rupture" or "explosive" break of the follicle. The follicular liquid seeps out very gently, and carries the ovum with it. Both the preovulatory swelling and ovulation itself are produced by the combined action of FSH and LH.

LH not only produces the development of the corpus luteum but is also responsible for its involution, as illustrated by the fact that the corpus luteum persists for months in hypophysectomized animals and is caused to involute only by the injection of LH.

Dr. Hisaw has been able to produce the estrus cycle in hypophysectomized animals artificially by using suitable doses of FSH and LH.

BOOK REVIEWS

THE COLON AS A HEALTH REGULATOR—FROM A SURGEON'S POINT OF VIEW. The Effects and Treatment of Its Developmental Abnormalities. Sir Henry M. W. Gray. 100 pp. Toronto: The Macmillan Company of Canada, Limited, 1936. $2.50.

There is much food for thought in this little book of exactly 100 pages, which is concerned entirely with the various types of intra-abdominal developmental adhesions, bands, kinks and malformations and their possible relation to certain rather vague clinical pictures with which all doctors are to some extent familiar. Surgeons have all seen these lesions but for the most part have considered them as variations from the normal, probably without clinical significance. Subhepatic adhesions (Harris's bands), Jackson's membrane, Lane's membrane and kink, parietocolic bands (both right and left-sided), unrotated cecum, cecum mobile, visceroptosis, omega sigmoid and several other conditions of like nature are discussed as causative factors in the production of definite symptoms which can be permanently relieved by the surgical correction of the abnormality. The discussion is quite impassionate, for the most part, and indicates a real interest and considerable knowledge on the part of the author concerning this thesis, on which he has worked for twenty-five years.

Six case histories are given as illustrative of the type of individual affected and the nature of the complaints. The first three, all women of 45 years and under, were nervous, irritable and constipated and complained of low abdominal pain. The type of operation performed is not stated, except for hysterectomy in the first. We can assume that various developmental adhesions were divided, as is definitely stated in the next three cases. The author describes his procedure as a "spring cleaning" operation.

He also suggests that these abnormalities may be causative factors in the production of definite, diseased conditions, such as stomach ulcer, appendicitis, cholecystitis, and so forth, and cites ten cases of gastric ulcer, in eight of which the ulcer disappeared following only appendectomy and proximal colopexy. Jackson's and Lane's membranes may cause appendicitis, and many periappendiceal adhesions are the cause and not the effect of appendicitis.

It is certainly true that there are many patients with vague abdominal symptoms not explainable on the basis of the usual recognizable pathologic conditions. Such people are a tax on the patience and diagnostic ability of their physicians, and the reader will recognize, in some of the author's descriptions, clinical pictures identical with some he has encountered in his own experience. If the author's surgery has produced these results, and if the relief of symptoms has not been due to other less obvious factors, then this book is a real contribution to surgery. In any event, it presents an accurate description of the different conditions mentioned and should stimulate constructive thinking and more careful observation of these intra-abdominal abnormalities when the abdomen is being explored in connection with common pathologic conditions.

SEXUAL POWER. Chester Tilton Stone. 172 pp. New York and London: D. Appleton-Century Company, 1937. $1.50.

This is an exuberant, discursive, prolix exposition of the manly art and practice of coitus. Because it attempts to define so protean a manifestation of virility, it extends from descriptive anatomy, through physiology, psychology, sociology, up to and even through philosophy. Here and there in the first two chapters, which are titled Impotence and The Psychic Basis of Sexual Difficulties, there is much sensible information concerning male potency and the usual underlying causes of impotence. Had the text stopped there, the book would be useful to clinicians and might even be helpful to many laymen, and laywomen, too, for there are many accurate animadversions to the female role. The third chapter on The Chemistry of Human Nature includes twenty-eight pages of what this critic considers endocrine nonsense. This and the two succeeding chapters on The Physical Basis of Sexual Difficulties and Sexual Efficiency are not quite unintelligible enough and so more than offset the value of the first part for lay consumption. The more discriminating, medically-trained reader would still be able, perhaps, to profit by the author's wide clinical experience in cases of male copulative difficulties and his serious consideration of causes and cures.

The book is nicely bound in cloth boards, and clearly printed. The text is pleasantly written and easy to read, but, especially in the latter half of the book, often perplexing and too frequently misinformative.

ON THE INCIDENCE OF ANAESTHETIC COMPLICATIONS AND THEIR RELATION TO BASAL NARCOSIS. C. J. M. Dawkins. 56 pp. London: John Murray, 1936. 3/6 net.

This monograph is based on an impressive array of tables arranged to show the relation of basal narcosis to postoperative complications (especially pulmonary complications) and mortality. Interest centers on 3,095 anesthesias between 1931 and 1935, in 505 of which basal narcotics were used. Apparently these were nembutal and pernocton, and apparently they were followed by inhalation anesthetics, but the text and tables are not clear on either point. The text also says nothing about routes of administration or about dosage, except that the drugs produced "sound sleep." (It is usually conceded that much heavier doses are used in London than are customary in this country.)

Postoperative pulmonary complications occurred twice as often with basal narcosis (11.1 per cent) as without (5.83 per cent), but the subsequent mortality was practically the same in the two groups (0.8 per cent and 0.77 per cent, respectively). Three cases of restlessness occurred after basal narcotics, and severe or prolonged vomiting was twice as frequent (1.2 per cent) as in the other group (0.61 per cent). No figures are given to show in which group the total morbidity from all types of complications was greater. It is likely that the author viewed his

statistics with a mind prejudiced against basal narcotics, for by totaling certain figures given in the tables the reviewer finds that nonpulmonary mortality was definitely lower in the basal narcotic group (3.1 per cent) than in the other group (4.3 per cent). The tables also show, although the text does not so state, that total mortality was less in the basal narcotic series (4.0 per cent) than in the other (5.1 per cent).

The author states that ether convulsions—much more common in England than in this country—are unknown following basal narcotics. However, the barbiturates may cause a variety of postoperative neurologic complications, as well as oliguria. Sodium amytal and pernocton intravenously are followed too frequently by postoperative restlessness and pulmonary complications, and nembutal by mouth is unreliable in action. Paraldehyde is the safest basal narcotic.

The advice given concerning the prevention of postoperative pulmonary complications is good. The items demanding attention are oral hygiene, postponement of operation in case of a cold, careful wrapping of the patient on the way to and from the operating room, temperatures of 75°F. or over in the operating room, minimal trauma and exposure of viscera, light general anesthesia combined with field block, the avoidance of inhaling of material, with the use of the intratracheal method and packing of the pharynx when indicated, and the avoidance of basal narcotics, of elevators for gall bladder or kidney operations and of tight bandaging.

MALADIES INFECTIOUS. Leçons Cliniques Profèssees a l'Hôpital Claude-Bernard. A. Lemierre. 307 pp. Paris: Masson et Cie, 1937. 55 Fr. fr.

This second volume on infectious diseases by Professor Lemierre contains seventeen clinical lectures. Such conditions as Hodgkin's disease with undulant fever, postarsphenamine hemorrhagic eruptions with fever, ulcerative pharyngostomatitis due to heavy metals, and leukemia are included. All of the subjects are well presented and discussed in considerable detail. A number of the clinics reflect the interest of the writer in anaerobic bacterial infections, including the *Bacillus funduliformis*, which has received only slight attention in this country. There is an excellent clinical discussion of a case of Weil's disease without jaundice. A case report of postabortive sepsis due to *Bacillus perfringens* is included, and the description of the clinical course of this disease is given, together with a review of the important literature bearing on the subject. The question of the existence of kala-azar in France is thoroughly discussed. Two clinics are devoted to the subject of malaria, particularly the form arising from inoculation of patients with general paresis.

It is of considerable interest to have a collection of clinical lectures on infectious diseases from France, since one has available in accessible form a description of various common and unusual conditions as they are observed in a large French clinic.

PHYSIOLOGY IN HEALTH AND DISEASE. Carl J. Wiggers. 1124 pp. Second Edition, Thoroughly Revised. Philadelphia: Lea & Febiger, 1937. $9.00.

The writing of a textbook by a single author results usually in coherence of plan and homogeneity of style; these advantages appear in this book. On the other hand, physiology has developed so extensively that it is not possible for any single person to evaluate duly the evidence and theories in the several specialized and relatively independent branches of the science. Since the author attempts to cover not only normal but also pathologic physiology, and endeavors to give up-to-date information in both fields, the difficulty is correspondingly increased. As a consequence some of the chapters, such as those dealing with the cardiovascular system, are better than others, such as those concerning the autonomic nervous system and some of the endocrine glands.

The book is intended to fulfill the needs of medical students, both those taking the course in physiology and those confronted later with clinical problems involving physiologic principles. It is also intended as a reference book for graduates, physiologists and clinicians. For the beginner there are probably many distracting pathological applications, and the development of some fundamental, normal processes is insufficient, for example, the role of the carotid sinus in the control of respiration. For the investigator any didactic textbook is elementary.

The book should be of great value to students and clinicians searching for orientation in problems of pathologic physiology. The presentation of the topics is clear and suggestive. The illustrations, tables and schemata are judiciously selected. The references are adequate for further information.

THE THYROID AND ITS DISEASES. J. H. Means. 602 pp. Philadelphia, Montreal, London: J. B. Lippincott Company, 1937. $6.00.

This book is the product of a clinic which has made valuable contributions to our knowledge of the diseases of the thyroid. Its introductory chapters on the development, structure and function of the thyroid contain in brief form nearly everything there is to be known of these aspects of the thyroid gland. Each following chapter is written on this same plan. The chapters have the additional advantages of being summarized at the end and followed by a most complete bibliography. Simple goiter, myxedema, juvenile myxedema in cretinism, toxic goiter, the relation of iodine to thyroid toxicity—all such states are simply and adequately presented in succeeding chapters.

A method of grading preoperative risks together with suggestions as to the management and preparation of each group is recorded under surgery of the thyroid. The reviewer has never been convinced that varying degrees of thyroid toxicity plus the added complications of associated heart lesions, liver damage and vascular changes lend themselves satisfactorily to any arbitrary grouping such as that described here. Neither could the reviewer find himself in sympathy with the suggestion that local anesthesia is in many ways the safest. It has been the conviction of the reviewer that local anesthesia adds to the difficulties not only of the patient but likewise of the surgeon. When one has available an anesthetic such as cyclopropane with its high percentage of oxygen, the advantage of having the patient soundly asleep without the disadvantage of the hitherto associated anoxemia is considerable.

The reviewer finds himself in complete agreement with most of the advice and the suggestions in connection with the actual surgery of subtotal thyroidectomy. The management of thyroid crises is adequate and sound.

The book closes with a very interesting and valuable chapter on Fact and Fancy in Matters of the Thyroid. There have been so many theories evolved regarding thyroid states that this chapter makes interesting and instructive reading.

This book might well have a few more illustrations since the subject of thyroid disease lends itself so well to illustrations, but on the other hand, it is largely the product of a medical group interested perhaps less in the striking illustrations which are obtainable with diseases of

the thyroid and more in the fundamental studies in connection with thyroid disease. It contains a large amount of valuable and trustworthy knowledge. It is a book to be read with profit by all who are interested in thyroid disease.

Biological Time. P. Lecomte Du Noüy. 180 pp. New York: The Macmillan Company, 1937. $2.00.

The main thesis presented in this book is that there are "two species of time." One of these is time as ordinarily considered, measured by the rate of the rotation of the earth. The other, "physiological time," is an individual sense of time in living organisms, and its rate depends on the rate at which certain fundamental processes take place. As examples of such processes the author selects cicatrization of wounds and the effect of blood serum on the duration of growth of fibroblasts in vitro. The older the individual concerned, the slower is cicatrization and the shorter the growth of cultures of fibroblasts. Since the two time scales do not coincide, astronomical time will seem, subjectively, to pass in inverse ratio, that is, much slower in youth and faster with age.

The subject of the mechanism of the appreciation of time is large and very few data bearing directly on it are available. One would welcome a serious study of the problem. The present book, however, can hardly be taken as such. Part I consists of a general discussion, in a colloquial style, of the philosophy of science, the personal attitude of the scientist, and the methods available for investigation of a problem, with their possibilities and limitations. In Part II the data are presented in a manner which proposes to demonstrate to the lay reader how a scientist's mind works. The author's own work on the development of a formula to describe quantitatively the rate of cicatrization of wounds is dealt with in some detail. Tissue culture studies are then described, solely on the basis of the work of Alexis Carrel, who wrote the foreword to the book, and his pupils. Harrison is dismissed as having failed to prolong the life of explants beyond a few days, Fischer is mentioned as the author of a volume on tissue culture technic, but no one else in the field is considered. The style verges on journalistic—"tremendous aseptic precautions," "marvelously perfected," "real talent, great manual dexterity, patience, and imagination," and so forth. Part III opens with a chapter on modern physical concepts of time and then proceeds with the main subject of the book. The data presented in Part II, which are obviously phenomena of aging of the individual, are applied to the problem of conscious appreciation of the passage of time. To bridge the gap "a passive, subconscious memory of physico-chemical or chemical nature" is invoked. Thus, in the midst of a good deal of excellent logical and mathematical juggling, the fundamental problem is buried in words.

In spite of several drawbacks, the book is interesting and presents a number of concepts and a point of view that may be utilized to better advantage in the future. It is not to be recommended to the layman, but rather to those members of the profession who enjoy reading the ideas of their fellow members for the fun of the ideas.

Diseases of the Nose, Throat and Ear. A Handbook for Students and Practitioners. I. Simson Hall. 423 pp. Baltimore: William Wood & Company, 1937. $4.00.

The writer of a book for students and practitioners is inevitably confronted with a difficult task if both classes of readers are really to profit in their use of such a book. The needs of a student who desires the presentation of many basic anatomic and physiologic facts are essentially different from those of a practitioner of medicine whose main interest must always lie along the lines of diagnosis and therapy. This dilemma is further increased in the case of a book on such a special subject as otolaryngology, since there here enters the additional problem as to whether "practitioner" means the general practitioner or the specialist, each of whom has entirely different needs with respect to a reference book.

If in addition such a book, purporting to meet a wide range of reader's requirements, is compressed into so small a space as to be designated as a "handbook," there inevitably result omissions and inadequate inclusions, which leave one somewhat in doubt as to its essential value to either student, general practitioner or specialist.

The author has made a gallant attempt to solve this difficult problem. The book is of a most convenient size and attractive format, and is reminiscent of the classic "Diseases of the Eye" by May. Illustrations, except for one colored frontispiece, are half-tones, many of which are quite English in their composition.

The arrangement is that of the larger and more complete textbooks, striving to include anatomy, physiology, diagnosis and treatment of all the recognized subdivisions of the specialty. To be thus forced into so small a book, to cover retropharyngeal abscess in half a page and labyrinthitis in little more, has resulted, from the standpoint of genuine utility to the reader, in including the subject only in order to avoid omitting it. Operative procedures are described and illustrated with corresponding brevity. This special field of medicine has become so wide that numerous textbooks now deal exclusively with such subjects as aural or nasal surgery, nasal physiology, endoscopy and chronic deafness. To compress all these into a handbook is, in spite of the present most creditable attempt, an almost superhuman task.

Quelques Vérités Premières (Ou Soi-Disant Telles) en Pneumologie Clinique. Émile Sergent. 84 pp. Paris: Masson et Cie, 1937. 24 Fr. fr.

This small, paper-bound volume is one of a group of similar publications under the title of "Collection des Vérités Premières." These, as the title indicates, are an attempt to put in very simple terms the outstanding accepted facts in various aspects of medical practice. The present one concerns the clinical aspects of diseases of the lungs and is written by Professor Émile Sergent, who is in charge of the introductory courses in clinical medicine at the University of Paris.

The author has attempted to emphasize the importance of good history taking and careful physical examinations in this field. It is the type of material which would constitute the introductory lectures in physical diagnosis, and might very well be used at the conclusion of the modern course in medicine to admonish students, who have been highly trained with the technical scientific implements, not to neglect the first principles of auscultation and percussion. The inadequacies of the special laboratory examinations, when they are not supplemented by a careful history and physical findings, are repeatedly emphasized and various specific pitfalls are pointed out. The material is divided into three chapters: Guiding Principles, which is a continuation of the introduction; Methods, including history taking, inspection with the naked eye and with the fluoroscope, palpation, percussion, auscultation, special direct examinations and finally, laboratory examinations; Special Syndromes, including asthmatic syndrome, syndromes of bronchitis and emphysema, pulmo-

nary syndromes (acute and chronic), pleural syndrome, mediastinal syndrome and diaphragmatic syndrome. In the latter chapter are included many helpful hints in history taking and in the simple examinations which are very useful in differential diagnosis.

The book, as a whole, is beautifully printed in very clear type and has the appearance of a volume of poetry. The French is very simple. It may be quite useful to American readers who have only an elementary knowledge of French and who wish to brush up on their French reading.

ACTA MEDICA SCANDINAVICA. Supplementum LXXVIII. Rapports et Comptes Rendus du Dix-Septième Congrès de Médecine des Pays du Nord Tenu à Copenhague du 27 au 29 Juin 1935. A. Norgaard. 941 pp. Copenhague: Imprimerie Royale Bagge.

This report of the 1935 medical congress of the Scandinavian countries is an impressive document demonstrating the significant role played by these nations in furthering progress in internal medicine. It includes 101 contributions with discussions. The communications are characterized primarily by the experimental and particularly the physiologic approach to the problems described. Experimental studies of the cardiovascular system represent a considerable portion of the report. There are several excellent studies (C. Sonne, B. von Bonsdorff, A. Jervell, G. Nylin, E. Bierring) on functional tests of the heart and of the circulation. Hematology is represented by contributions bearing on iron deficiency in certain cases of pernicious anemia; by studies on blood regeneration (expressed in a simple equation); by a study of the bone marrow in relation to eosinophilia; and so forth. Several significant contributions are reported on various aspects of arthritis.

It is particularly encouraging in these days, when medical investigation is rapidly declining in several European countries, to see the torch of science carried ahead in countries in which free thinking is still practiced. It is hoped that through the wider dissemination of such reports as this a closer exchange of medical ideas between the Scandinavian countries and this country will be established.

SURGICAL PATHOLOGY OF THE THYROID GLAND. Hertzler's Monographs on Surgical Pathology. Arthur E. Hertzler. 298 pp. Philadelphia, Montreal and London: J. B. Lippincott Company, 1936. $5.00.

Dr. Hertzler's monograph is interestingly written and attractively presented. It is based on his very large experience and is not too hampered by acceptance of traditional thesis. The well-chosen illustrations add much to the value of the book. To some of the hypotheses put forth and treatments advised the reviewer cannot subscribe, but knowing the marked variation in thyroid pathology induced by geographic and other factors, he is hesitant to criticize a sincere opinion based on careful and multitudinous observations.

One thesis, however, seems definitely dangerous, namely, to quote from the preface, "If removing a part of a diseased gland is beneficial to the patient, what is more logical than to assume that removing the whole will be better? To remove the whole gland is simple enough now that we have freed ourselves of the Kocher fetish of cachexia thyropriva. It has become merely a question of technic." The author has picked up whole-heartedly, and apparently advises carrying to its logical, though perhaps not desirable, extreme, the doctrine of total thyroidectomy.

Chapter VII, The Cardiotoxic Goiter, the reviewer has more difficulty in viewing with equanimity than other portions of the book. The conclusion that the hyperthyroidism associated with Hashimoto's disease is due to the "action of the acinal cells characteristic of this disease" is not in accordance with generally accepted facts.

In all, this book can be recommended to the practitioner interested in thyroid disease from the standpoint of a wealth of material presented in a somewhat challenging manner.

QUELQUES VÉRITÉS PREMIÈRES (OU SOI-DISANT TELLES) SUR LES MALADIES DU FOIE. Noël Fiessinger. 79 pp. Paris: Masson et Cie, 1936. 24 Fr. fr.

In these days of long and wordy monographs, it is a pleasure to read a concise presentation of the maladies of a given system. The author, Fiessinger, in presenting the primary topic of diseases of the liver, gives an exceedingly clear picture of the various aspects of biliary tract disease. The little volume is free from statistical data and charts and from controversial discussions. The presentation, however, is scintillating, and has very few omissions. The style is epigrammatic, and many of the phrases and sentences are so pithy that the facts and the discussion of them are easily grasped.

The entire field of biliary tract disease is ably covered and includes comments on diagnostic procedures, the symptomatology of hepatic disease, and treatment. Numerous fads and hobbies are quickly disposed of, and the treatise is full of the wisdom gained only by a prolonged experience in the diagnosis and treatment of disease. The ideas expressed in the book, with few exceptions, are up to the minute, but are always conservative and always sound. The book is easily read in a short time. In many ways it is one of the most brilliant and concise expositions of a difficult diagnostic and therapeutic field that has appeared. Its chief, but not its only value, lies in its brevity and in the conciseness of its remarks.

THE MORPHINE HABIT AND ITS PAINLESS TREATMENT. G. Laughton Scott. Second Edition. 105 pp. London: H. K. Lewis & Co., 1937. 5s.

This little book describes a special method of morphine withdrawal by the substitution of atropine or belladonna. It presents Dr. Scott's particular method of treatment, and in addition to the atropine substitution, he devotes considerable space to the general management of the addict. Brief case histories of twenty cases are given, and he states that he has treated a great many more. As an appendix there is the testimonial of a physician who has been treated by this method. It seems strange that this work has not appeared in any of the standard journals of medicine and that no references are given to any original data. If one accepts his data as given, the method seems to have merit.

His chapter on the physiology and pharmacology of atropine is a little startling at first reading, but if his theory is well founded, it represents an important pharmacologic fact which is neglected in the usual text. In brief, it consists of overwhelming the peripheral depression of parasympathetic nerve endings by an increase in the central stimulating effect of the drug. He explains the use of this drug as a substitute for morphine by asserting that withdrawal symptoms are largely concerned with the absence of vagal stimulation produced by morphine and that the withdrawal is rendered easier if such stimulation can be continued. The theoretical aspects of this method are of sufficient importance to merit more vigorous controlled experiments in support of the thesis.

DR. BODO OTTO AND THE MEDICAL BACKGROUND OF THE AMERICAN REVOLUTION. James E. Gibson. 345 pp. Springfield and Baltimore: Charles C Thomas, 1937. $4.00.

Dr. Bodo Otto, a German immigrant, played a not inconspicuous part in the American Revolution and, because of this and other interesting features of his life, has long deserved a biography. Mr. Gibson has given us an excellent book, from which we can get a true portrait of an energetic, sound, loyal citizen, who had a wide influence on the practice of medicine in Pennsylvania and whose work in the Revolutionary War was of such a character as to leave a record unblemished when compared with the active personal conflicts of such men as Rush and Shippen. His letters and reports throw new light upon Shippen and lead us to believe that many of the charges put forth by Rush, which led to a court-martial, were unfounded. Thus, because of the material contained in this book, Shippen's character grows and Rush loses something of his greatness. Mr. Gibson, after many years of research, has brought to light original documents on this controversy and many other features of medical life during the Revolution.

The greater part of the book, fortunately, is taken up with this material, the life of Dr. Otto being only a framework upon which to erect the structure of sound textual criticism. The reviewer knows of no book in which more authentic information on the medical side of the Revolution is contained, and it is hoped that medical historians will not be turned away from what would at first appear to be a biography of a relatively unimportant man, thereby missing material of great importance. Well-written and nicely published, this book is one of the most important ever published in the medical literature of the American Revolution.

A TEXT-BOOK OF MENTAL DEFICIENCY. (AMENTIA.) A. F. Tredgold. 556 pp. Sixth Edition. Baltimore: William Wood & Company, 1937. $7.50.

This volume is the latest edition of a work which was first published in 1908. Throughout this period it has been regarded with respect, and its present revision is adequate. Dr. Tredgold presents the experience and the point of view of the worker in institutions in Great Britain, and quite inevitably, the volume is of special value to those who are engaged in institutional practice.

The author is convinced that at least 70 per cent of the mental defects are primary. However, he does not believe that any practicable plan of birth control or of sterilization will cause any great reduction in numbers.

There is very little information about the pathologic changes and no mention of the value of encephalography as a diagnostic or prognostic measure. The adequacy of the general discussion is so genuine, however, that the book is valuable to anyone whose work brings him into responsible contact with this important field of medicine.

THE CARDIAC GLYCOSIDES. A series of three lectures delivered in the College of The Pharmaceutical Society of Great Britain under the auspices of the University of London. Arthur Stoll. 80 pp. London: The Pharmaceutical Press, 1937.

The author records his chemical and pharmacologic studies of the cardiac glucosides, called in this monograph, glycosides. The study is similar to that employed by him in the isolation of active principles in squill. It is his particular thesis that the Balkan *Digitalis lanata* has a higher glucoside content than the ordinary red foxglove or *Digitalis purpurea,* and that the former contains an additional glucoside which he names C. He has succeeded in separating three glucosides and obtaining them in chemically pure crystalline form. He states that a mixture of these contains all the therapeutic and a minimum of toxic effects, that it is stable, and that it may be administered intravenously and intramuscularly. He presents no biologic assays of his own, but refers to one paper in the literature. No clinical evidence is presented, but reference is made to one recent article.

CONTRIBUTIONS TO THE MICROSCOPIC ANATOMY OF THE PANCREAS. Paul Langerhans. Reprint of the German Original with an English Translation and an Introductory Essay. H. Morrison. 39 pp. Baltimore: The Johns Hopkins Press, 1937. $1.00.

This compact reproduction and translation of the classic of Langerhans on the "Microscopic Anatomy of the Pancreas" is one that should be in every medical library and the library of every physician interested in medical history.

The straightforwardness and accuracy of this description of the pancreas, in which the islands were recognized for the first time, is an excellent example of careful study.

Both the translator and the publisher are to be commended for this contribution.

CLINICAL LABORATORY DIAGNOSIS. Samuel A. Levinson and Robert P. MacFate. 877 pp. Philadelphia: Lea & Febiger, 1937. $9.50.

One is impressed on the first reading of this book by the tremendous scope of the work attempted. It is not amazing that the printed text should number eight hundred and thirty-eight when one glances over the chapter headings: The Mouth; The Stomach; The Duodenum and Liver; The Intestines; Metabolism; Chemical Analysis of the Blood; The Kidneys; Chemical Analysis of the Urine; Hematology; Immunology and Serology; Cerebrospinal Fluid; General Bacteriology; Skin Tests and Other Biological Examinations; Laboratory Methods in Pediatric Procedures; Milk and Water Analysis; Histological Technic; Legal Medicine and Toxicology; Appendix; Special Appendix.

The book, as noted in its preface, is an elaboration of a small volume which has been in use in the University of Illinois College of Medicine by students in clinical pathology. The authors' purpose in presenting this edition is to give the student, intern, practicing physician and technician a "suitable review of clinical laboratory diagnosis sufficient to meet their general needs."

The contents of the book supposedly represent clinical tests concerning practically the entire body. The outline of their presentation is fairly uniform—first, method of procedure; secondly, evaluation of results; thirdly, clinical application or interpretation. Satisfactory detail in many instances is lacking, though much valuable information is furnished. Certain important laboratory procedures are given accurately and clearly. Unfortunately, the presentation leaps from peak to peak, and is not fundamentally sound, because few men are able, or willing, to take the time required to search elsewhere for other data, often vital to their particular problems, which it is assumed they already know.

The book cannot be recommended unqualifiedly. For the laboratory technician and the student in medicine it offers much of value; for the man in general practice or the internist it fails in its avowed purpose.

THE NORMAL ENCEPHALOGRAM. Leo M. Davidoff and Cornelius G. Dyke. 224 pp. Philadelphia: Lea & Febiger, 1937. $5.50.

Encephalography was introduced into medical practice in 1919 by Dandy, who also is credited with introducing ventriculography. Because of the ease of doing encephalography by injecting air into the lumbar subarachnoid space through the usual lumbar puncture, it has replaced ventriculography, or the direct injection of air into the ventricles, as a routine diagnostic procedure in neurologic clinics. There are certain circumstances where ventriculography is much superior to encephalography, but for the usual examination of the subarachnoid space and the ventricular system the more simple encephalography is sufficient. It is now widely used in cases in which there is a suspected deformity of the brain, ventricles or the subarachnoid space. So little was known about the conformation of these structures in a normal person before the introduction of these studies that a new conception of the fluid spaces of the brain has been developed, and the normal relations of these spaces to the brain substance itself are the subject of this fine monograph by Davidoff and Dyke. They, working together as neurologist and radiologist at the Neurological Institute of New York, have reached a high degree of efficiency in the interpretation of both the normal encephalogram and the encephalogram as it is modified by structural disease of the brain or its coverings.

This short book, with a historical introduction, deals with the methods used for encephalography, including the roentgenographic technic and considerations in regard to the absorption of gas and the possible therapeutic effects of the procedure. There follow individual chapters on the appearance of the normal ventricles and other structures, the cerebral convolutions and their sulci, and the subarachnoid cisterns. Following these is a final chapter, in which the individual organs of the brain are considered in relation to the fluid spaces. The book is profusely illustrated with photographs of brain specimens and x-rays. There is an extensive bibliography and index. As the basis for interpretation of the normal encephalogram this book will be indispensable to both the neurologist and the roentgenologist. It is understood that the authors have a companion volume on the pathologic encephalogram, which is to be published shortly.

CLINICAL ROENTGENOLOGY OF THE CARDIOVASCULAR SYSTEM. Hugo Roesler. 343 pp. Springfield and Baltimore: Charles C Thomas, 1937. $7.50.

This volume of 343 pages with nearly 200 illustrations is an unusually complete and detailed presentation. The fundamental facts in anatomy, physiology and pathology, together with some original experiments and the common clinical applications of roentgenology of the cardiovascular system, are adequately described. The author approaches the subject from the standpoint of a roentgenologist who has turned cardiologist. Criticism may be offered by those who wish a short cut or a more easily readable book. Critical analysis of the literature has not been offered, but it is apparent that all of the literature has been painstakingly considered in the preparation of this work. A discussion of the various types of cardiac measurements, kymography, congenital heart disease, pericardial disease, peripheral vascular disease and other less common subjects is included.

This book will be found to be of definite value to the roentgenologist and the cardiologist.

THE BASIS OF CLINICAL NEUROLOGY. The Anatomy and Physiology of the Nervous System in Their Application to Clinical Neurology. Samuel Brock. 360 pp. Baltimore: William Wood & Company, 1937. $4.75.

In the preface to this excellent book by Dr. Brock, one of the neurologists at the Neurological Institute of New York, he states: "The past teaches us that the abstract neurophysiology of to-day becomes an instrument of clinical neurology to-morrow." With this statement every neurologist will agree and because of the great growth of neurophysiology and its importance to the man in practice, books such as this are of the greatest possible value. Here one finds the literature, so widely scattered in numerous publications, abstracted and brought together in a convenient form. For the student, as well as the practitioner, this book becomes an invaluable source for either a review of current neurophysiology or as a basis for research. Dr. Brock has seen fit to separate his monograph from a textbook on clinical neurology, a stand which will be greatly appreciated by all. The subject has become so great that to combine modern neurophysiology and clinical neurology is a task beyond the scope of any single individual.

QUELQUES VÉRITÉS PREMIÈRES (OU SOI-DISANT TELLES) EN PATHOLOGIE CARDIO-VASCULAIRE. E. Donzelot. 82 pp. Paris: Masson et Cie, 1937. 24 Fr. fr.

This is a collection of aphorisms on the diagnosis and treatment of cardiovascular disease written by a distinguished French professor. A superb typographical arrangement involving the exclusive use of capitals and italics hurls each hardy generalization at the reader with the force of a thunderbolt from Olympus. One finds little that is new but many old observations, newly and succinctly phrased.

ANNUAL REPRINTS OF THE REPORTS OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR 1936, with comments that have appeared in the JOURNAL. 104 pp. Chicago: American Medical Association. $1.00.

This book is essentially a record of the negative actions of the Council on Pharmacy and Chemistry of the American Medical Association; that is, it sets forth the findings concerning medicinal preparations which the Council has voted to be unacceptable for recognition and use by the medical profession. Many of the reports record outright rejection or the rescinding of previous acceptances; others report in a preliminary way on products which appear to have promise but are not yet sufficiently tested or controlled to be ready for general use by the profession.

NEW AND NONOFFICIAL REMEDIES, 1937. Containing descriptions of the articles which stand accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1937. 557 pp. Chicago: American Medical Association, 1937. $1.50.

The annual editions of this volume contain all that the busy physician needs to know concerning the newer preparations which he is daily importuned by the detail men of the pharmaceutical manufacturers to use. The remedies listed and described have been examined and found acceptable by the Council on Pharmacy and Chemistry, the deliberative body charged by the American Medical Association with the performance of this service for the practitioner, who has not the time or means to make the determinations for himself.